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Original Communications

CIRCULATION IN THE MATERNAL PLACENTA OF PRIMATES*

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WHEN a worker in the basic sciences has the temerity to present his findings to a clinical group, especially if he is reporting upon animal investigations, an apologetic note frequently creeps into the presentation. It is not because of immodesty that the traditional apologies are here lacking, but rather because those working at the Carnegie Laboratory in Baltimore have constantly before them a classic example of the fact that the mere monkey can be an invaluable tool to clinical workers in the field of human reproduction. This classic example is the so-called "monkey yardstick" which Streeter and Heuser[1] worked out at Carnegie in the early 1930's at the time when young human embryos were as scarce as the proverbial hen's teeth and were only acquired haphazardly, with inadequate or inaccurate histories and often in fragments or unsatisfactorily prepared. One thinks of the three isolated sections of the Miller ovum,[2] of the single section of the Kleinhans[3] or the pathological Bryce-Teacher[4] which embryologists tried for years to fit into a classification because they did not know enough about the normal to recognize the abnormal. At that time it occurred to Streeter to capitalize on the known similarity of early embryonic development in the macaque to that in the human being and he devised a program of operative procedures which supplied an integrated series of accurately dated, technically satisfactory monkey specimens. Against this "yardstick" of thoroughly studied monkey embryos it was possible to measure the human specimens acquired and to determine their age and relative stage of development. Then when the great Hertig-Rock[5] embryos came along the yardstick was ready to help in their classification and interpretation.

*Presented before the Brooklyn Gynecological Society, March 18, 1953.

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Since pregnant human uteri at various stages, with the placenta in situ, are almost as hard to obtain as early embryos, work was commenced at the Carnegie Laboratory some years ago to set up a similar monkey yardstick for the placenta. The purpose of the study has somewhat broadened as time has passed. Initially the question to be answered was: "How do the endometrial blood vessels, whose behavior during the nonpregnant cycle had been well worked out by Bartelmez,[6] Daron,[7] Markee,[8] and others, adapt themselves to the conditions of pregnancy?" Subsequently, as clinical interest intensified in the question of the marginal sinus and its role in antepartum hemorrhage, a detailed investigation of this structure and of placental venous drainage in general was added to the field of study.[9, 10]

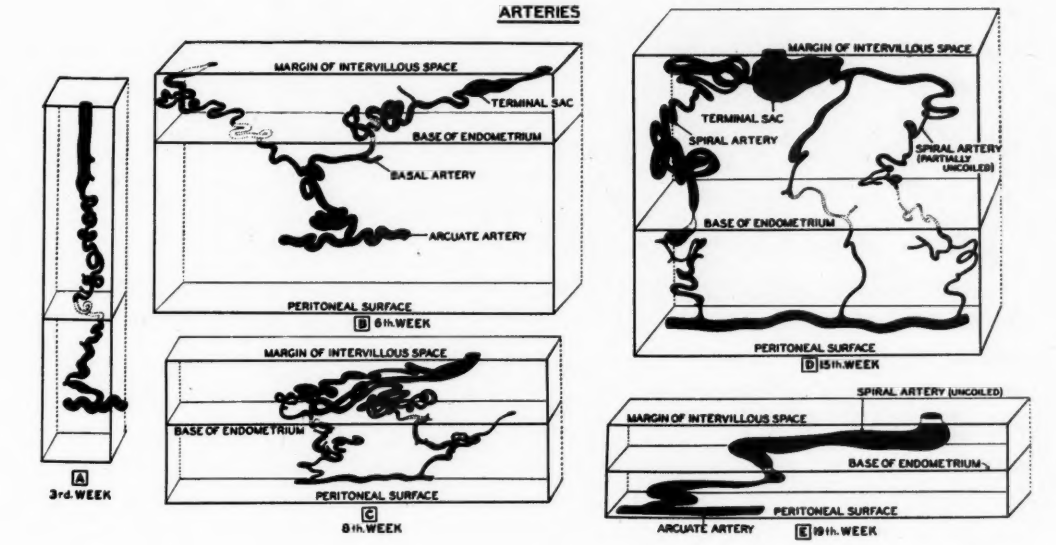
There is no intention of implying that the monkey findings to be reported here are replicas of conditions in the human being nor that any conclusions regarding placental circulation in the macaque can be transferred bodily to the interpretation of human physiology and pathology. The human placenta must be worked out for itself, just as the early human embryo had to be worked out; for the various primate groups are only similar, not identical. However, since significant similarity does exist, there is marked advantage in the study of a limited quantity of monkey material obtained under optimum and controlled circumstances, planned with the production of satisfactory specimens as the sole consideration. Such conditions cannot be expected of clinical material in which the welfare of the patient rather than the state of the tissues is necessarily the determining factor. As a result, the average clinical material, despite its abundance, is of dubious value when scientifically examined and screened, and fully acceptable specimens are exceedingly rare. Hence the usefulness of the "monkey yardstick" which provides a background of seriated, well-studied macaque material against which the study of human material becomes easier and can be carried out with the smaller available quantity of satisfactory human specimens. The accumulation of suitable human material in the Carnegie Laboratory is in progress and more than a dozen in situ placentas of various stages, injected under controlled conditions, are already in hand. To this human material occasional reference will be made, but, in general, since the extended human study contemplated is not yet completed, all remarks and illustrations in this report are based on the monkey unless specifically stated otherwise.

Technique

Twenty-three rhesus monkeys (*Macaca mulatta*) were employed in this study (Table I). All were members of the Carnegie colony and had been palpated for ovulation and bred at specific dates. On the desired day of pregnancy, the monkey was anesthetized and India ink was injected via a cannula in the aorta. When the injection of the uterine vessels was complete, the anesthesia was deepened until the animal died. The entire reproductive tract was immediately removed and fixed in formalin. Thereafter large blocks were cut from representative portions of the uterus, invariably embracing the full thickness of the placenta and uterine wall, and were embedded in celloidin preparatory to serial sectioning at 50 μ. Sections were stained with hema-

toxylin and eosin. The number of blocks prepared and sectioned in any given specimen was determined solely by the necessity for achieving sufficient visualization of the vascular pattern to permit generalization. The total series consists of between 6,500 and 7,000 sections. Three-dimensional reconstructions of representative specimens were prepared by the cellophane sheet modification of the glass plate method.[9]

Fig. 1.



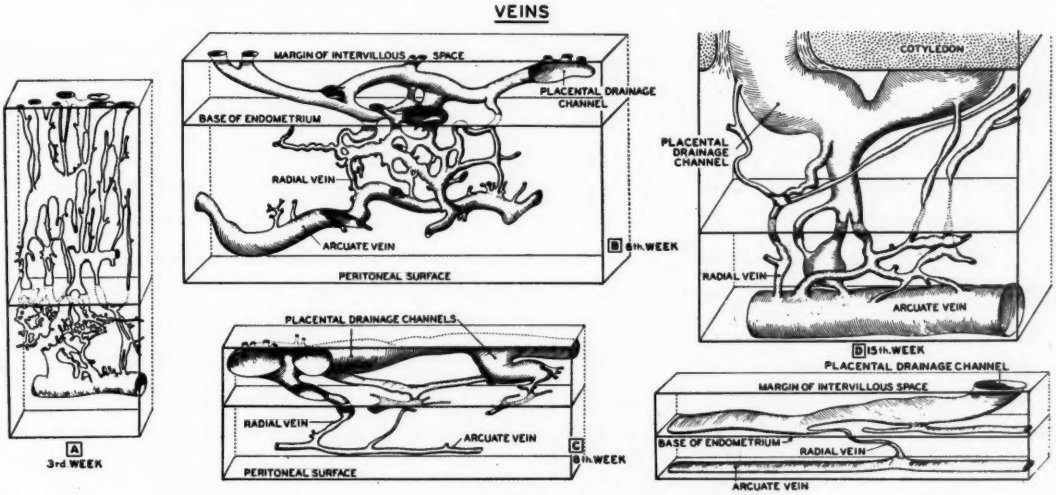


Fig. 2.

Figs. 1 and 2.—Diagrammatic representations of the course and configuration of the spiral arteries and the veins of the maternal placenta at various stages of pregnancy; based upon three-dimensional reconstructions of serial sections.

Results

To the question proposed at the outset of these studies, "How do the endometrial blood vessels react to the mechanical and hormonal stimuli of an implanting and developing ovum?" the following answer was obtained.

TABLE I. DURATION OF PREGNANCY IN ANIMALS USED

Usual gestation period in *M. mulatta:* about 165 days

MONKEY NUMBER	DAY OF PREGNANCY	MONKEY NUMBER	DAY OF PREGNANCY
C 651	19	C 731	95
C 649	22	C 679	102
C 658	38	C 711	102
C 608	50	C 721	103
C 629	53	C 710	108
C 604	66	C 699	110
C 730	74	C 680	127
C 727	79	C 733	129
C 615	80	C 732	145
C 616	90	C 686	154
C 709	90	C 713	156
C 700	91		

Course of the Spiral Arteries.—

During the progestational phase of the cycle, as various studies have shown,[6, 7, 8] the endometrial coiled arteries grow rapidly toward the uterine lumen, at the same time becoming increasingly coiled. When implantation occurs, the arterial tips still lie some millimeters below the surface epithelium, but slightly before the nineteenth day (ovulation age), continued arterial growth plus trophoblastic invasion effects an opening of maternal arteries into the intervillous space of the placenta. Thereafter, continued growth of the trophoblast opens up progressively more spiral arteries which accommodate themselves to the reduction in endometrial thickness occasioned by pressure and encroachment of the overlying conceptus, by increased coiling as well as by back-and-forth and lateral looping.

As development progresses, small branches of the spiral arteries and some of the straight basal arteries assume major proportions and enter the intervillous space as independent stems, or, conversely, various adjacent stems may coalesce close to the intervillous space and enter it by way of a common dilated terminal sac.

Beyond the fifty-third day the spiral arteries do not materially increase in length and there is no further significant alteration in their course for another 5 to 7 weeks until, at about the ninetieth day, the pregnant uterus undergoes the great transformation known as "conversion." The recognition and interpretation of this important phenomenon was the work of Samuel Reynolds of the Carnegie Laboratory.[11] It is the phenomenon which occurs when uterine accommodation of the products of conception ceases to be effected primarily

Fig. 3.—Extensive endothelial proliferation is seen at *A* in a spiral artery just before its entrance into the intervillous space. A vein at *B* shows a lesser degree of endothelial proliferation. Monkey C477, twenty-ninth day of pregnancy. (×150. Reduced one-fourth.)

Fig. 4.—A spiral artery is seen at its point of entry to the intervillous space (right) and two cross sections of a more proximal coil of the same vessel are seen at the left. Pronounced endothelial proliferation is apparent and there is beginning epithelioid transformation of the cells of the media. Monkey C658, thirty-eighth day of pregnancy. (×30. Reduced one-fourth.)

Fig. 5.—Intimal fibrosis almost completely occludes the lumen of an artery in the mid-endometrium (*A*); constriction of an arterial lumen without intimal fibrosis is seen at *B* and *C;* epithelioid change in the media of an artery appears at *D* at a stage of pregnancy when endothelial proliferation has disappeared. Monkey C679, one hundred and second day of pregnancy. (×25. Reduced one-fourth.)

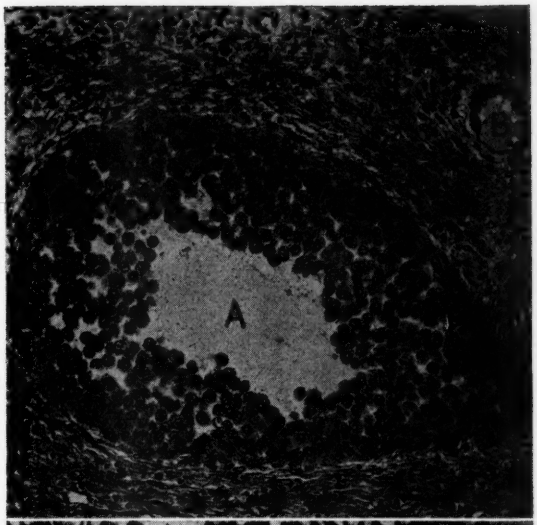


Fig. 3.

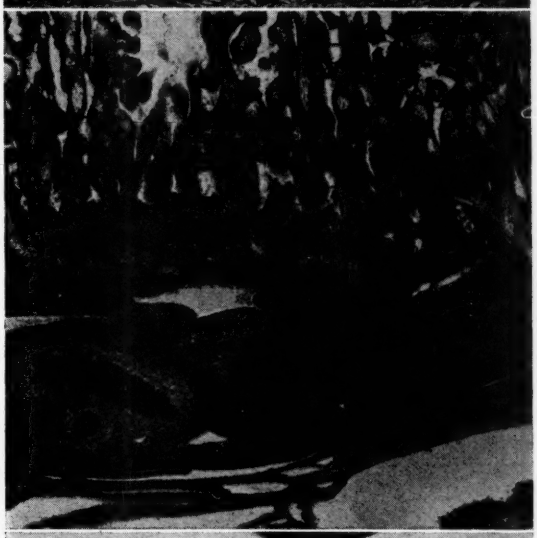


Fig. 4.

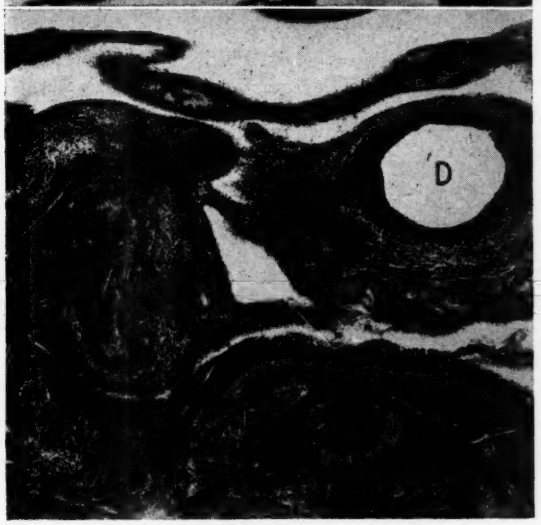


Fig. 5.

(*For legends, see opposite page.*)

by uterine growth and commences to be upon the basis of uterine stretching. At this critical point the uterus is converted from spherical to cylindrical form. Concomitant with this conversion in shape the coils of the spiral arteries are paid out, much as lengths of rope coiled up on the deck of a boat may be paid out. At the same time the number of arteries communicating with the intervillous space is decreased. Following conversion the course of the remaining placental arteries, now a smooth, direct one interrupted only by an occasional right-angled bend, remains unchanged up to term (Fig. 1).

Walls of the Spiral Arteries.—

Certain important histological changes in the walls of the arteries accompany these changes in course and in all probability are the basis upon which they take place. In the first few days following implantation of the macaque ovum, a striking wave of proliferative activity brings about hyperplasia of endothelium in capillary, venous, and arterial channels (Fig. 3). Initially this involves only the tips of the spiral arteries, but the process gradually progresses proximally and is sufficient to diminish the caliber of the lumen very markedly (Fig. 4). In addition there is a progressive replacement of muscle cells in the media and adventitia by epithelioid cells (Figs. 4 and 5). In the latter portion of pregnancy the endothelial proliferation wanes but the medial change persists. Intimal fibrosis is a final feature which makes its appearance around the fifty-third day, is markedly accentuated at the time of conversion, and persists up to term (Fig. 5). Of variable extent, sometimes completely and permanently obliterating a stem or narrowing the lumen of another, the fibrosis is largely responsible for the reduction in number of arteries communciating with the intervillous space after conversion.

Venous System.—

The course of the veins is subject to less elaborate modifications during pregnancy than that of the arteries. Other than the initial brief period of endothelial hyperplasia, there are no important cytological changes (Figs. 3, 9, 10, and 11). Like the arteries, however, the veins are subjected to the erosive action of the trophoblast, which creates a multitude of openings through which, by reflux flow, the first maternal blood reaches the intervillous

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Fig. 6.—The margin of the attached placenta to show characteristic paucity of villi in the marginal sinus and continuity of the latter with the subchorial lake. The overriding of the placental margin and application of the fetal membranes deep into the angle between placenta and decidua vera can be readily made out. The narrowness of the marginal sinus at this level is to be contrasted with its dimensions in Fig. 7, 115 sections removed. Monkey C710, one hundred and eighth day of pregnancy. (×6. Reduced one-fourth.)

Fig. 7.—The same placenta as that seen in Fig. 6 at a level 115 sections removed, to show the variations in marginal sinus size within one and the same placenta. Overriding is pronounced. There is peripheral lobulation with a placental septum at the point of constriction. A serpentine venous channel winds through this septum. Its point of free communication with the marginal sinus occurs several sections later in the series. Recently formed thrombi occupy the lower fourth of the intervillous space on the right. Monkey C710, one hundred eighth day of pregnancy. (×6. Reduced one-fourth.)

Fig. 8.—Over-all view of the marginal region of the placenta in situ showing continuity of the marginal sinus with the subchorial lake, paucity of villi in the marginal sinus, and a small unorganized thrombus at its base. Overriding of the placental margin has been obliterated by secondary fibrous adhesion. At *X* is the point of entry into the intervillous space of a spiral artery, its location unusually far toward the periphery. The orifice of exit of the large vein cut in oblique section occurs at the point *Y*, 10 sections earlier in the series, close to the base of a septum of which a portion is seen to the right of *Y*. A second venous exit is seen at the extreme right. Monkey C686, one hundred fifty-fourth day of pregnancy. (×6. Reduced one-fourth.)

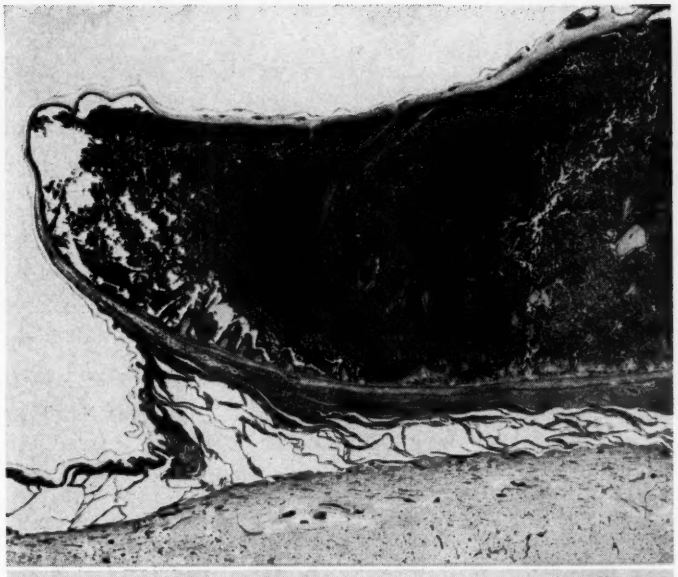

Fig. 6.

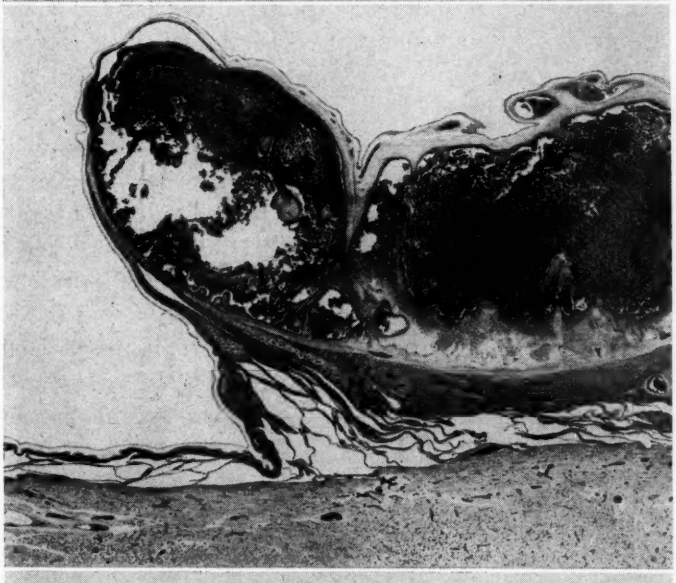

Fig. 7.

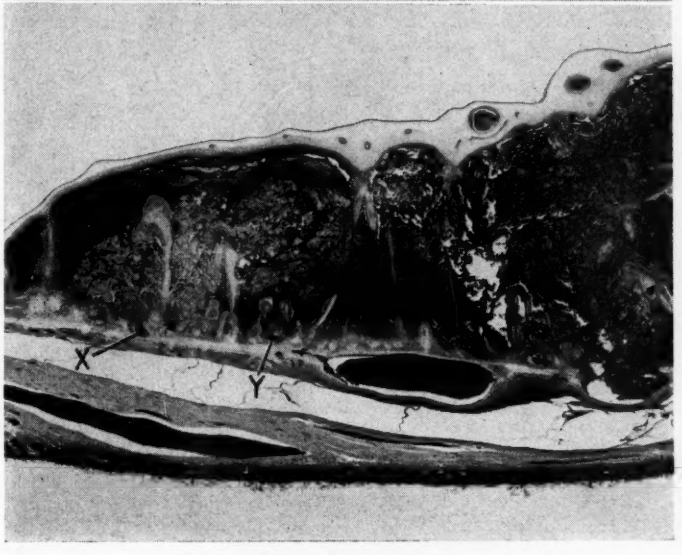

Fig. 8.

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space shortly after implantation, nearly a week before arterial communication is established. By the end of the first month, the number of venous exits from the intervillous space commences to decrease, the smaller passages being gradually pinched off by pressure from without. Lacking coils of extra length to pay out, such as the arteries have, the veins accommodate themselves to "conversion" by a fairly simple stretching which narrows the channels, irons out localized dilatations, and produces ribbonlike horizontal or arcuate channels connected with the great myometrial veins by short radial segments of narrow caliber (Fig. 2).

Marginal Sinus.—

So far nothing has been said about the marginal sinus to which attention must now be turned. In the first place, what does the marginal sinus look like? Even more basically, *is* there a marginal sinus? This is an assumption which several qualified observers deny.[12, 13] If there is one, how is it drained? And, finally, is it the sole route of placental drainage as maintained by Spanner[14] and his followers?

To the basic question, the present macaque material supplies an affirmative answer. In every placenta from an animal pregnant for more than 6 weeks adequate search revealed a definite and distinctive marginal sinus. Contrary opinions seem to have arisen for the most part owing to confusion of terminology, inadequate materials, and the use of delivered instead of in situ placentas.

In the sense in which Spanner[14] and most contemporary workers use the term (Falkiner,[15] Fish,[16] Earn and Nicholson,[17] Harris,[18] Hertig,[19] Hellman,[20] Hamilton and Boyd,[12] etc.) the marginal sinus is the peripheral portion of the intervillous space (Figs. 6, 7, and 8). It is not a separate vessel running around the margin of the placenta, as is frequently assumed. It is the marginal portion of the intervillous space itself, bounded laterally by the chorionic membrane, below by the trophoblastic plate, and above gradually merging with the subchorial lake. Centrally it merges with the rest of the intervillous space. No constant septum or wall separates it from the central portion of the placenta. The structure is thus maternal, not fetal, and lies within the placenta, not within the endometrium. It is variable in size and form since its dimensions and character are profoundly influenced by the quantity of blood present in the intervillous space at any given time as well as by the pressure to which it is subjected. Villi are characteristically sparse within the marginal sinus (Figs. 6, 7, and 8) and marantic thrombi frequently occur within it, indicating a sluggish circulation (Figs. 7 and 8).

Fig. 9.—Two basal venous orifices are seen located, respectively, 3 and 3.5 cm. in from the placental margin at a level where the entire placental diameter is 8 cm. Monkey C709, ninetieth day of pregnancy. (×10. Reduced one-fourth.)

Fig. 10.—A large venous channel is seen pursuing a short course directly from the intervillous space to the myometrium. The orifice in the trophoblastic plate lies 3.5 cm. in from the margin of a placenta measuring 10 cm. in diameter at this level. Monkey C686, one hundred fifty-fourth day of pregnancy. (×20. Reduced one-fourth.)

Fig. 11.—A vein is seen traversing the cobweb-thin endometrial spongiosa of a postconversion specimen. The orifice in the trophoblastic plate is just equidistant between the placental margin and the point of attachment of the umbilical cord. Monkey C731, ninety-fifth day of pregnancy. (× 6. Reduced one-fourth.)

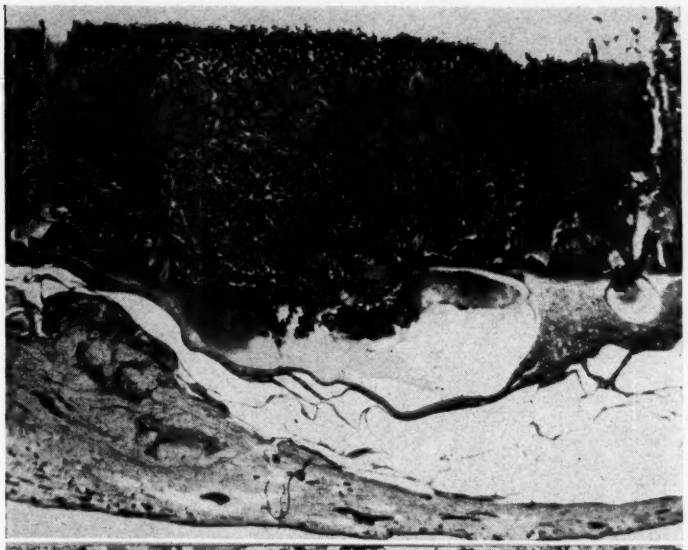

Fig. 9.

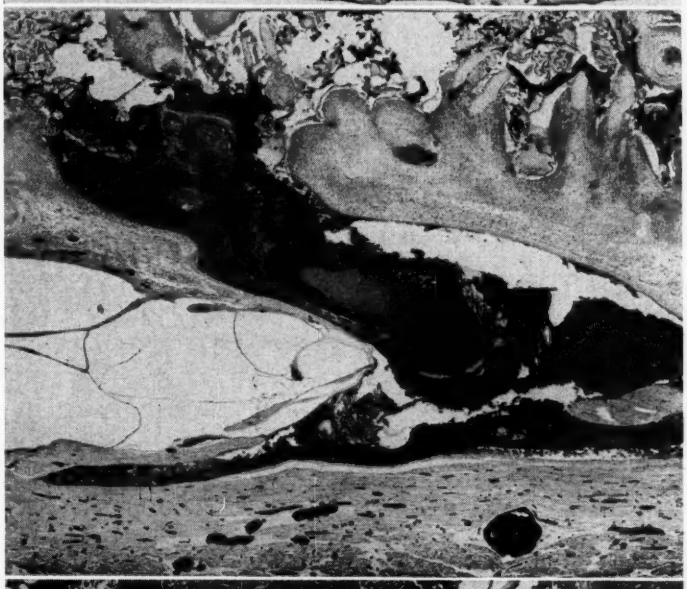

Fig. 10.

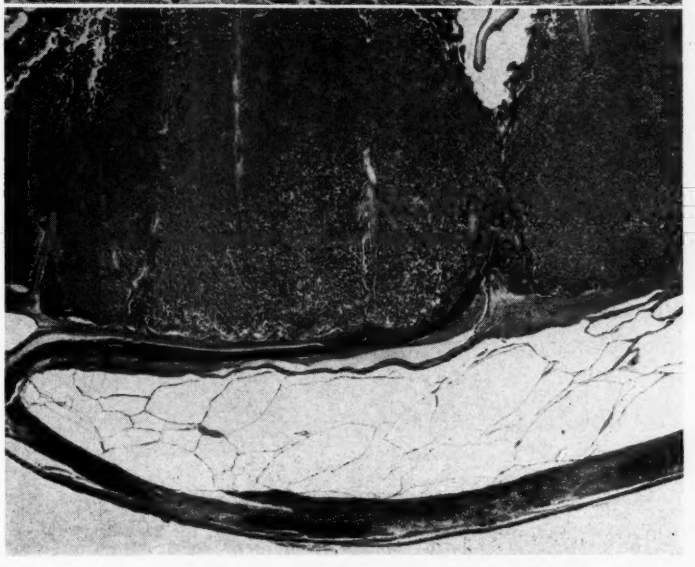

Fig. 11.

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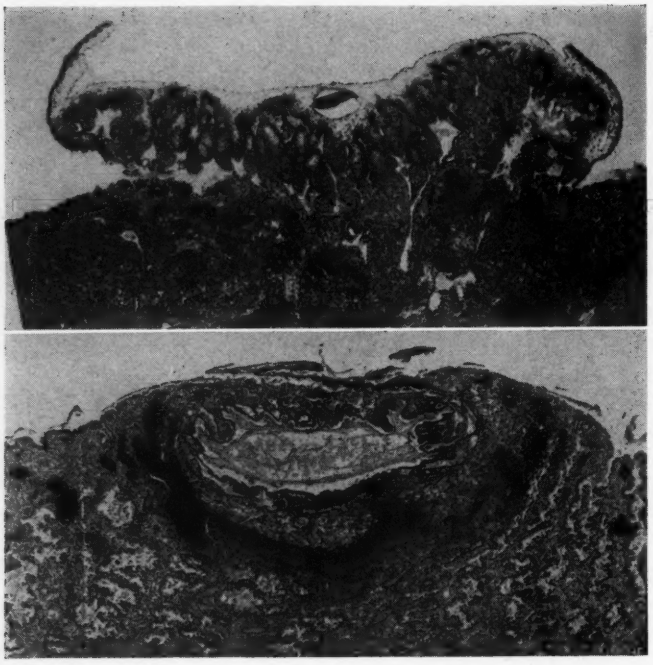
A.



B.

Fig. 12.—Monkey and human conceptuses of comparable age to show superficial versus interstitial implantation.

A, Monkey, fifteenth day of pregnancy. Pronounced umbilication of placental base with overriding of the decidua vera at both margins. Monkey C571. (×24. Reduced one-fourth.)

B, Human, fourteenth day of pregnancy. The blastocyst lies below the endometrial surface. The marginal regions are in contact with the decidua and its vascular constituents. Yale Embryo.[23] Carnegie No. 6734. (×14. Reduced one-fourth.)

Fig. 13.—Entrance of a spiral artery into the intervillous space is seen at the center of the photomicrograph. The afferent stream of ink rises part way to the chorion with little lateral seepage. A relatively inkless zone surrounds the rising stream with accumulations of ink again seen at the periphery on both sides. Subsequent sections show these to be coursing toward venous exits. Monkey C733, one hundred twenty-ninth day of pregnancy. (×6. Reduced one-fourth.)

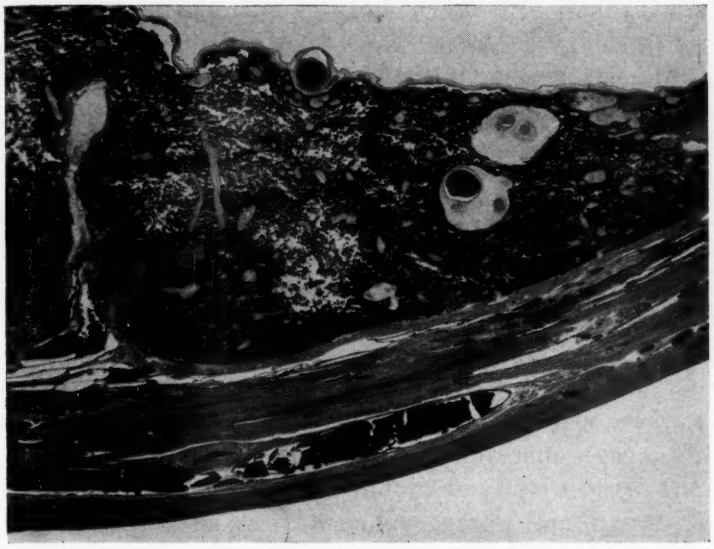


Fig. 14.—Marginal region of an injected human placenta in situ from the seventh month of pregnancy. Drainage of the marginal sinus is here effected by the venous channel on the far left which perforates the trophoblastic plate at the base of an incomplete placental septum. Carnegie No. 8695. (×5. Reduced one-fourth.)

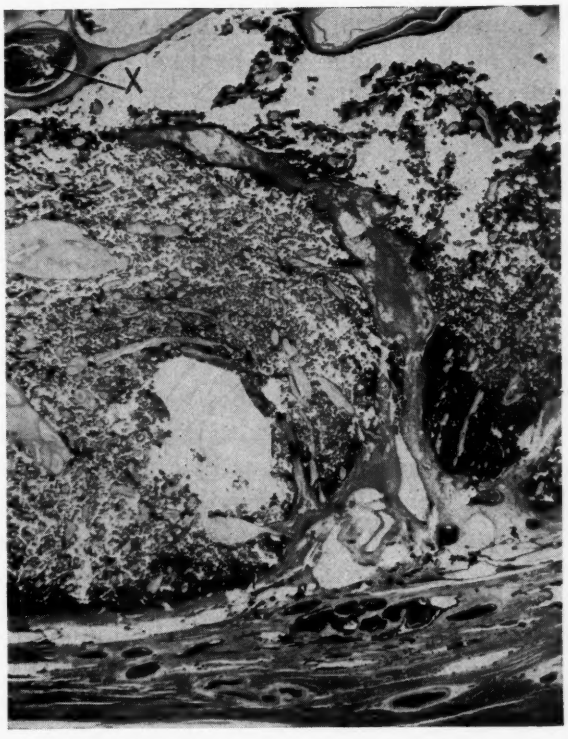


Fig. 15.—Central portion of the same placenta as in Fig. 14. The point of attachment of the umbilical cord is seen at *X*. To the left of the incomplete placental septum a maternal vein starts its course down through the decidual plate. Carnegie No. 8695. (×5. Reduced one-fourth.)

The marginal sinus of the monkey is not drained directly, i.e., by vessels proceeding straight out of it down into the endometrium to connect with maternal veins. Instead, the veins which drain the marginal sinus cross the trophoblastic plate in a zone 1 to 1.5 cm. in from (central to) the placental margin (Fig. 8). Spanner saw this indirect form of marginal sinus drainage in the human being but considered it of less importance than the direct sort. Preliminary studies of the injected human placenta in situ are in agreement with Spanner on this point (Fig. 14). The difference between human and monkey drainage patterns apparently goes back to the early days of intrauterine life and is dependent upon the difference in type of implantation, superficial in the macaque and interstitial in the human being (Fig. 12).

For another and far more important opinion of Spanner's, confirmation has not been found either in the monkey or in the human. Spanner firmly contends that there are no central basal drainage channels in the mature placenta—or only a rare, anomalous one, and that drainage is exclusively via the margin. In the present study an abundance of centrally placed veins has been seen, studied, drawn, and photographed in both species. Statistics have not yet been compiled in the human being, but in 19 monkeys at various stages of pregnancy from 50 days to term, 63 placental veins have been fully traced, of which 36 were basal and 27 marginal. In both basal and marginal locations there is a strong tendency for bunching of channels. This fact might account for failure to note them if only a small series of sections was studied and those sections happened to fall between bunches.

In addition issue must be taken with Spanner's concept of placental septa as fluid-tight dividers. In the present study of the monkey the septa were found to be incomplete and richly perforated, and so incapable of delimiting a blood stream (Figs. 7, 14, and 15).

Comment

The fact that abundant basal drainage of the mature placenta exists makes necessary a re-evaluation of the widely popular Spanner theory of placental circulation. Spanner, it will be recalled, envisages overflow filling of the placenta with arterial blood which is introduced by the spiral arteries through orifices in the trophoblastic plate and rises between the septal walls to the subchorial lake before spreading laterally to the marginal sinus through which all venous drainage of the placenta takes place. In the absence of effective septal dividers, we must conclude (1) that there is no inviolable channel conveying the arterial blood to the subchorial lake, and (2) that lateral seepage is therefore possible. Furthermore, since venous exit points often lie fairly close to arterial entries, doubt is cast upon the essential features of the Spanner theory and we are left with the problem: Why doesn't the arterial blood short-cut from entry to adjacent exit without rising in the placenta and circulating through it, among and around the villi, as it must do to achieve metabolic exchange?

The injected specimens of the present series provide an opportunity to trace the masses of India ink into and out of the intervillous space (Fig. 13).

In many instances the complete separation of ink streams which are fairly close neighbors can be demonstrated for a score or more of sections. It is apparent that the separation is accomplished, in the absence of septal dividers, by a process similar to the familiar separation of clear and muddy streams entering a grassy marsh where admixture occurs but slowly, despite the lack of any more fluid-tight dividers than the innumerable, irregularly spaced clumps of mud and grass. In the placenta, the villi act in similar fashion. The impetus for rise of arterial streams in the intervillous space is provided by the driving force of the maternal blood pressure. Between myometrial contractions, this exceeds the pressure in the intervillous space by 60 to 70 mm. Hg[21, 22] and may at times be augmented, if intermittent constriction of spiral arterioles continues throughout pregnancy, as much morphological evidence suggests.[9]

If the driving force of maternal blood pressure accounts for the discrete afferent streams of ink and blood coursing toward the subchorial lake, the convergence of efferent streams upon venous orifices is to be ascribed to the pressure within the intervillous space. The presence in the marginal sinus and in the basal trophoblast of blind pockets containing India ink or stagnant blood with laminated cellular elements indicates that much blood is forced into the marginal sinus and back to the basal plate at a distance from any venous exits and only slowly finds its way toward them. Such side-tracked blood or ink may be traced through long meandering courses to its confluence with active streams leading to venous outlets. Maintenance of venous flow within the uterine wall, preventing the building up of pressure within the intervillous space, is enhanced by myometrial contractions throughout pregnancy.

The marginal sinus, in answer to the questions posed earlier, does exist but it is not the sole portal, in either man or monkey, through which the intervillous space drains. In the monkey, it is not even a direct portal and the frequent occurrence of marantic thrombi within it shows that it is not a constant seat of vigorous circulation. Indeed, in the monkey, at least, it appears to play the role of a diverticulum or safety reservoir interposed in the course of the flow.

Summary

The following generalizations apply to the rhesus monkey and are based on study of 23 injected, in situ placentas of *Macaca mulatta* pregnant for periods of time ranging from 19 to 154 days:

1. During the period of growth, the endometrial arteries lengthen and become increasingly coiled. In the period of stretching which follows "conversion" the coils are paid out.

2. Endometrial veins grow less extensively than do the endometrial arteries and adapt to both phases of uterine enlargement chiefly by passive alterations in caliber.

3. The marginal sinus is constantly recognizable after the sixth week of pregnancy. Its drainage is largely indirect.

4. Basal drainage channels persist to term and are responsible for at least half of the venous drainage of the placenta.

5. Overflow filling of the placenta is achieved by the force of maternal blood pressure, which exceeds the pressure in the intervillous space by 60 to 70 mm. Hg, rather than by the action of septal dividers.

Certain comparisons between the placenta of the monkey and that of the human being are incorporated in the discussion.

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POSTPARTUM CERVICAL CARCINOMA*

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THIS study of 1,500 postpartum patients was instituted and completed in the postpartum clinic of Cook County Hospital, Chicago. A review of current literature fails to disclose any like study, any similar series of proved cases of cervical carcinoma. Our survey covered 18 months, extended from February, 1951, through October 31, 1952.

Our routine procedure was to have patients return for examination six weeks after delivery. Each patient was placed in lithotomy position, the cervix exposed by unlubricated speculum, then carefully examined under a strong light. All cervical lesions, erosions, polyps, eversions, etc., are subjected to biopsy, preceded by the Schiller Iodine Test, after which the postpartum examination is completed.

This study was made to determine if undetected cervical carcinoma, existing during pregnancy might at this six-week interval be discovered.

Of the 1,500 postpartum women subjected to this routine examination 226 presented cervical lesions, an incidence of 15.1 per cent. Two of these 226 lesions were carcinomatous, a percentage of 0.89. One was invasive, the other a preinvasive carcinoma. The final diagnosis in the other 224 was chronic cervicitis, chronic endocervicitis and either quiescent or healing cervical erosions. The over-all carcinoma incidence in these 1,500 women, therefore, was 0.14 per cent.

Diagnosis in the patient with invasive carcinoma was relatively simple. Three pathologists confirmed the findings. Diagnosis in the patient with preinvasive carcinoma was no more difficult, microscopically, the loss of cellular polarity, nuclear chromatin disturbance, disorder of nuclear cytoplasmic ratio, and abnormal mitotic figures being readily seen. These are the criteria upon which diagnosis of preinvasive carcinoma is predicated. Such findings, in a postpartum cervix, insist upon a diagnosis of carcinoma in situ. Our experience coincides with that of Schiller who declares that, once such changes occur, they are irreversible; this in contradistinction to those changes of epidermization and metaplasia, which are reversible.

Serious difficulty was experienced in but one biopsy specimen. This was a tangential cut of a cervical lesion presenting metaplasia of the endocervical glands with epidermization (Fig. 1). Four competent pathologists studied the disputed area of the slide. One diagnosed carcinoma in situ. One diag-

*This investigation was supported by a research grant from the Dr. Jerome D. Solomon Research Foundation, Hektoen Institute for Medical Research.

nosed early invasive carcinoma. Two diagnosed epidermization with metaplasia of the cervical glands. This patient, a 21-year-old Negro woman, gravida i, para ii, delivered twins at 32 weeks of gestation. Delivery was by outlet forceps and version and extraction, respectively. Cervical inspection at the time of delivery revealed no abnormalities. Six weeks post partum,

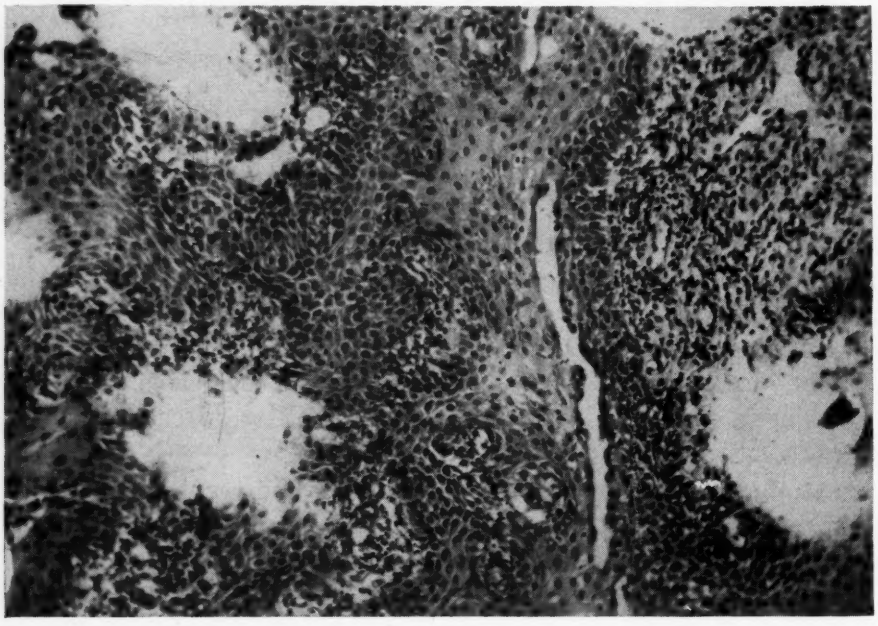

Fig. 1.—O. J., aged 21 years. Original cervical biopsy revealing epidermization associated with a healing cervical erosion, six weeks post partum. (×285. Reduced one-third.)

we discovered a cervical erosion. Cytologic smear finding was "abnormal cells, group 3." Biopsy strongly suggested "early invasive carcinoma." As this patient was but 21 years old, and we were unable to demonstrate other changes in the cervix, she was kept under close supervision and study in our postpartum clinic. Repeated cytologic smears were negative. No gross change in the cervix could be demonstrated. Confronted with disagreement among the pathologists as to exact diagnosis, fearful that indecision on our part might jeopardize early extirpation of the in situ malignancy, if such it actually were, we transferred her to our surgical service. Diagnostic curettage and circumferential biopsy of the cervix were carried out. Curettement was negative. Serial sections of this biopsy were negative for either invasive or preinvasive carcinoma. This patient remains under constant observation. Study during the past six months has revealed no cytologic change and she is now five months pregnant.

This case illustrates the great difficulty encountered in diagnosis in instances of metaplasia and epidermization, difficult not only for obstetrician or gynecologist, but likewise for well-qualified pathologists. Seemingly it does prove that epidermizations and metaplasias are reversible lesions. Our

experience leads us to theorize that this is the particular group wherein greatest confusion exists, where diagnosis of preinvasive carcinoma demands intensive study.

Carrow and Greene[1] recently stated that, as regards epidermization and metaplasia, similar changes are present in the cervix in both pregnant and nonpregnant women. Our experience coincides. However, we stress the importance of submitting every suspicious biopsy to not one, but to a minimum of three or four well-trained pathologists. In this manner each individual case can be painstakingly evaluated, ideal and optimum therapy determined upon, and maximum end result achieved.

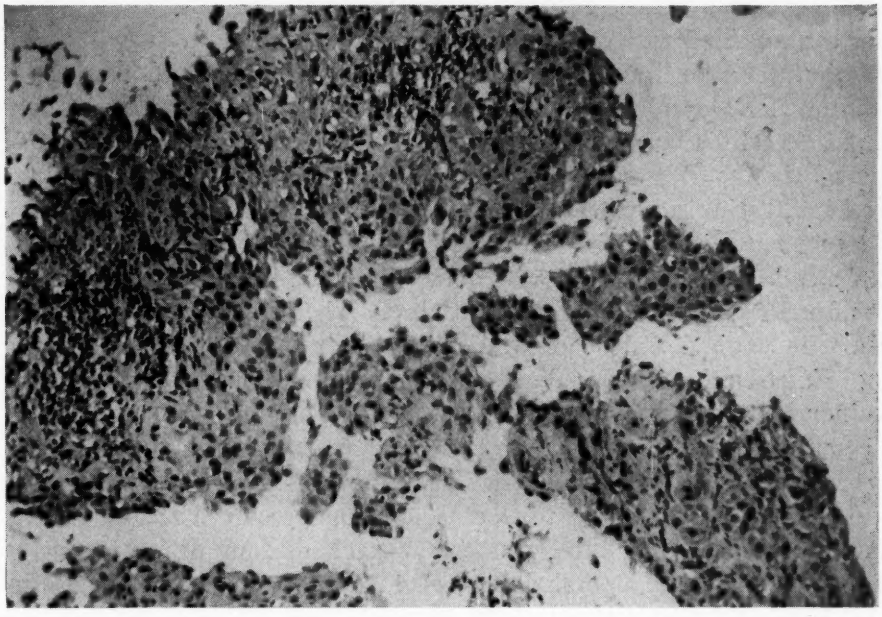

Fig. 2.—R. W., aged 38 years. Original cervical biopsy specimen. Infiltrative squamous-cell carcinoma. (×285. Reduced one-third.)

Papanicolaou, Traut, and Marchetti[2] demonstrated specific pregnancy change in their cytological studies. Following the discovery of the second case in our series, simultaneous investigation of both smear and biopsy was made part of our standard examination.

Our study shows that, about six weeks post partum, there is a small, well-defined group who show persistence of some abnormal, not necessarily malignant, basal cellular changes. This is the group so easily misinterpreted by the some-time cytologist, the group where differential diagnosis may be exceedingly difficult. Once these particular cells have been attentively studied, recognized, and classified properly, needless alarm can be avoided. In one group of 20 such patients whom we studied, these cells were found in the original smears. Concomitant biopsy disclosed no other abnormality other than that of severe erosion with coincident epidermization. Following smears at later dates revealed complete absence of these identical cells.

One bothersome case which amply demonstrated the need for early examination and prompt treatment was that of a 38-year-old Negro woman, gravida iv, para iv, who was admitted to the hospital Nov. 29, 1950, in active labor, and delivered a term infant. She stated she had had prenatal care during her pregnancy. Questioning brought out the fact that her local physician seemingly had never made a vaginal examination. Upon discharge she was instructed to return to the postpartum clinic six weeks later for further examination.

She returned on March 22, 1951, nearly four months later, because of the presence of a foul-smelling, bloody vaginal discharge that had begun two weeks previously with the cessation of menstruation. Speculum examination revealed the cervix almost completely replaced by a necrotic, fungating mass, that on contact bled easily and freely. Pelvic examination demonstrated the corpus, the uterosacral and paracervical tissues to be free. Biopsy was taken immediately. No cytologic smear was made. The patient was instructed to return to the clinic the following week. She was told that diagnosis would be known then and treatment would be instituted. Biopsy findings were "Stage I infiltrating squamous-cell carcinoma" (Fig. 2).

Despite her promise, she did not return. Written appeals, personal calls by staff members, repeated visits by police availed not at all.

On June 15, 1951, almost 4 months after her first postpartum visit because of the vaginal discharge, and nearly 7 months after delivery, she did return. Examination disclosed that the malignancy had advanced to "Stage II carcinoma of the cervix."

She was referred for x-ray and radium treatment. She was given, in a single application, 4,000 mg. hr. of radium (50 mg. for 80 hours). Beginning June 10, 1951, and continuing to Oct. 14, 1951, she received a total of 44 x-ray treatments, divided as follows: eleven to each of four different ports, two anterior, two posterior, a total dosage of 4,200 r to each port. Beginning on Nov. 14, 1951, and continuing to Dec. 18, 1951, 2,600 r were delivered through a perineal port. On March 21, 1952, and continuing to April 18, 1952, 3,700 r was given to each sacrosciatic port. Within this ten months' period the combined tumor dosage delivered by external radiation amounted to 5,700 r to each parametrium.

Chronologically the disease advanced as follows: In March, the diagnosis was "Stage I infiltrating squamous-cell carcinoma," the cervix almost completely replaced by a fungating mass. By June it advanced to a "Stage II." By September involvement and necrosis of the left vaginal fornix were evident. October examination revealed the necrotic area of the cervix extending from 12:00 o'clock to 4:00 o'clock, with induration of the left paracervical tissues. By November the left paracervical and uterosacral tissues were fixed. A necrotic, debris-covered crater with hard edges replaced the left one-half of the cervix; extension of the pathology to the right was unmistakable.

On May 14, 1952, she had a sudden, severe vaginal hemorrhage. She was at once hospitalized for control of bleeding. Examination of the cervix at this time strongly suggested a "Stage III, radioresistant cervical carcinoma."

Cystoscopic and proctoscopic examinations were negative for direct extension. On June 20, 1952, pelvic exenteration was carried out. Grossly the carcinoma seemed limited to the pelvis, there being no evidence of extension to either bowel or bladder. Recovery was uneventful. The pathological report revealed the endometrium and cervix involved with a diffuse necrotic ulceration by a gray necrotic tumor mass, infiltrating squamous-cell carcinoma, and involvement of both bladder base and rectum through to the mucosa of each.

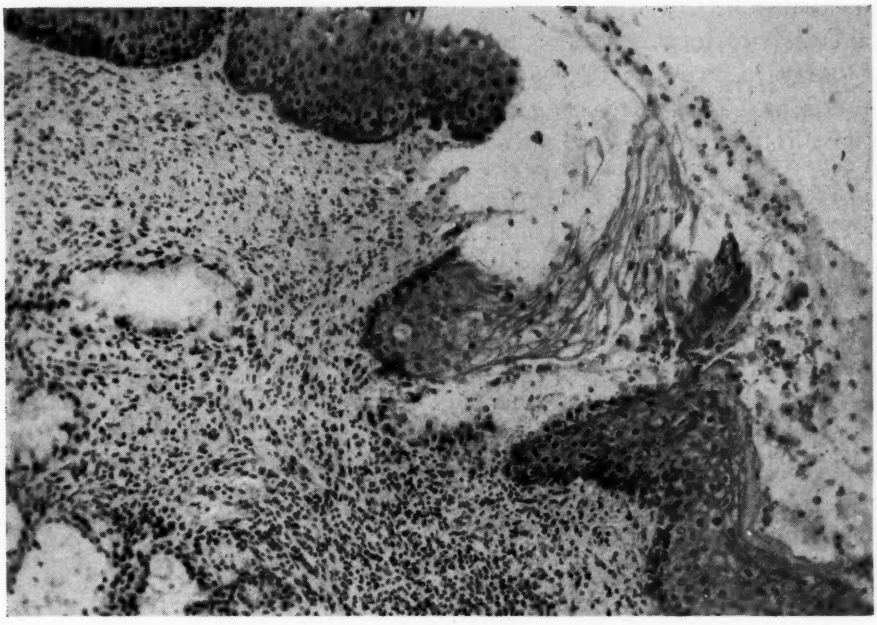

Fig. 3.—H. C., aged 34 years. Original cervical biopsy revealing carcinoma in situ in six weeks post partum cervix. (×285. Reduced one-third.)

Another instance which demonstrates the advantage of prompt examination was that of a 34-year-old Negro secundigravida who had spontaneously delivered a 3 pound, 1 ounce infant approximately six weeks prior to her clinic visit. She had a menstrual period and had no complaints. Speculum examination disclosed a small erosion of the posterior cervical lip. Biopsy revealed "carcinoma in situ" and no cytological smear was made (Fig. 3). She was hospitalized. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was carried out. Postoperative sections of the cervix were positive, diagnosis being "carcinoma in situ."

No test procedure, however accurate, is of any value unless it can be applied. To do this we must educate women to come to us, irrespective of age, pregnancy, or nonpregnancy. Immediate, accurate diagnosis in all instances of cervical lesions must be made before any therapy can be instituted. Only in this manner can the true incidence of cervical carcinoma be determined. This remains unknown and early recognition of malignancy is imperative if we are to lower both mortality and morbidity. No treatment should be given in any instance of cervical lesion until both smear and/or biopsy findings are

entered in the permanent record of the patient. That this examination will, in the great majority of patients, prove negative for malignancy is admitted, but such negation of findings in no wise justifies neglect to utilize every possible means of diagnosis in early malignancy. That responsibility is individual.

The detection of carcinoma in the routine postpartum examination has been demonstrated. A great deal of time, money, and effort is devoted in this country in educating and directing women to the medical profession for periodic examination for the detection of cancer. Since women voluntarily present themselves for this final obstetrical examination, it affords an unsurpassed opportunity to stress to the young patient the importance of future periodic examinations. These periodic examinations offer an excellent opportunity for the early detection of carcinoma. Herein lies the hope of eradicating this disease.

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EPITHELIAL ABNORMALTIES OF THE CERVIX DURING PREGNANCY*†

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IT IS widely accepted that pregnancy causes specific epithelial changes in the cervix and that these changes may be confused with preinvasive carcinoma. This belief has been nurtured by reports that such untreated preinvasive lesions have disappeared following termination of pregnancy. Epperson and coworkers[1] reported 5 of these lesions which apparently disappeared. Nesbitt and Hellman,[2] in a continuation of this work, added 2 more for a total of 7. Brown and Jernigan[3] followed 5 patients with a biopsy diagnosis of preinvasive carcinoma through pregnancy. Three of the 5 lesions persisted and 2 apparently disappeared. Hirst and Brown[4] reported one case discovered during pregnancy in which the lesion could not be found at postpartum hysterectomy. G. A. Hahn, in discussing this paper, mentioned another case which apparently disappeared post partum. The same case was mentioned previously by Dr. L. C. Scheffey in discussing a paper by Danforth.[6] Hoffman and others[5] described a case (apparently the same one mentioned by Scheffey and Hahn) "diagnosed invasive carcinoma in the third month of pregnancy by a consultant pathologist," which could not be found post partum. They did not, however, agree wholeheartedly with the original diagnosis. Unfortunately, the magnification of the photomicrograph and its poor quality of reproduction make interpretation difficult. The paucity of adequate photomicrographs of the lesions in all these papers is surprising when one reflects that the diagnosis of this lesion is subject, in certain instances, to such wide individual interpretation.

Danforth[6] and Murphy and Herbut[7] have been frequently misquoted as having observed such lesions to disappear. Review of these reports reveals that neither Danforth nor Murphy and Herbut found any preinvasive carcinomas among their patients and, therefore, could present no data on this problem. Indeed, one of the latter authors (Herbut) thought it wise to emphasize in his discussion that though the squamous epithelium does undergo change in pregnancy (a nonspecific thickening of all the layers and glycogen deposition) "this change does not in any way approach anything that resembles a carcinoma or a carcinoma in situ." Others[8, 9, 10] have made similar observa-

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†Presented at a meeting of the Chicago Gynecological Society, March 20, 1953.

TABLE I. PREINVASIVE CARCINOMA IN PREGNANCY

PATIENT NO.*	DATE†	AGE‡ GRAV. PARA.	ANTEPARTUM WEEKS	ANTEPARTUM SMEAR	ANTEPARTUM BIOPSY	POSTPARTUM WEEKS	POSTPARTUM SMEAR	POSTPARTUM BIOPSY	HYST. OR CONE	COMMENTS
15 B. B.	June 1952	20 G 1 P 1	28 32 36	Atyp. Pos.	 (2) Ca.	9	Pos.	(4) BCH		Unfortunately, cervix cauterized because of bleeding after last biopsy.
16 E. B.	April 1952	25 G 4 P 4	20 23 27 30	Atyp. Atyp.	 (1) Neg. (4) Ca.	24	Neg.	(4) Ca.		
17 M. G.	May 1951	27 G 4 P 4	6 7 8 36 37	 Pos.	(1) Ca. * * *	7 32 34 37	 Neg.	* * 	Ca. (Hyst.)	Abdomen opened, pregnancy discovered at time of third biopsy. Only the biopsy at 6 weeks and the hysterectomy specimens have been examined by us. * indicates biopsies not seen by us.
18 E. H.	May 1952	29 G 5 P 5	18 21 32	Pos. Pos. Pos.	 (4) Ca.	12	Atyp.	(4) Ca.		
19 H. S.	June 1952	25 G 5 P 4	24 28 34	* Neg. *	(1) Ca. (1) Neg. (2) *	4 8	Atyp.	(4) Ca.	Ca. (Hyst.)	Biopsy at 28 weeks was a cervical polyp. *Smears and biopsies not seen by us.

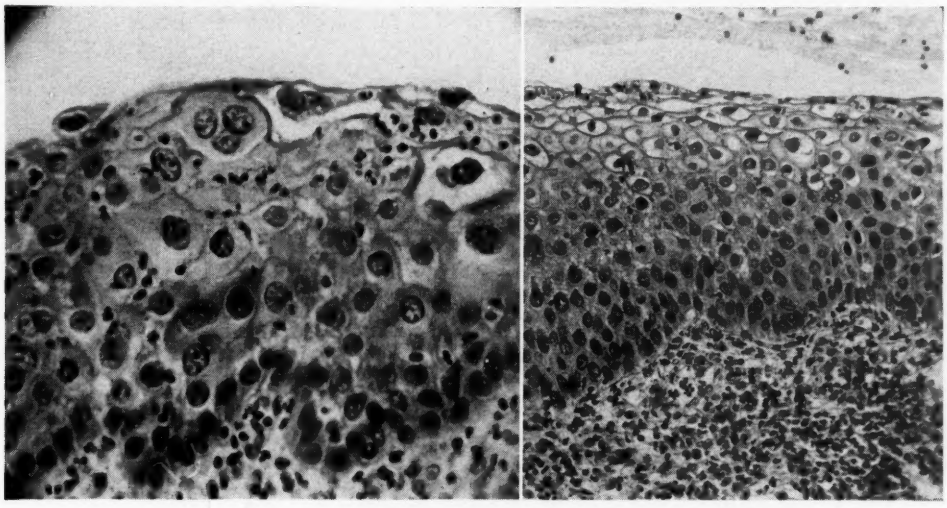
Atyp.—Atypical; Pos.—Positive; Neg.—Negative; Ca.—Preinvasive carcinoma; BCH—Atypical basal-cell hyperplasia; Hyst.—Hysterectomy; Cone—Cone type cervical amputation. The numbers in parentheses preceding the biopsies refer to the number of quadrants biopsied.

*Numbered consecutively to 14 cases previously reported.[11]

†Month and year of first smear or biopsy.

‡Age at first smear or biopsy; gravidity and parity after last pregnancy.

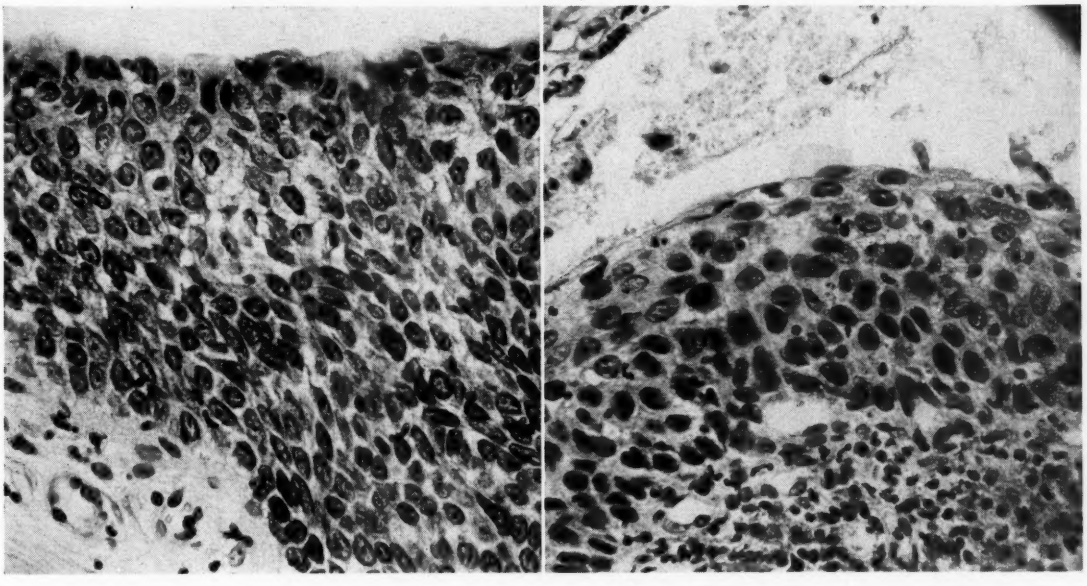
tions. He went on to say, "It follows, therefore, that if a pregnant woman has a lesion in the cervix, and if this lesion appears carcinomatous, then it probably is carcinoma and that patient had better be treated for it."



A. *B.*

Fig. 1.—*A*, Patient 15, NUMS No. 17137. Antepartum biopsy at 36 weeks. A well-differentiated preinvasive carcinoma of minute size found in only one quadrant. Bizarre bi- and trinucleate cells were frequent even in the superficial layers. The postpartum biopsies showed only a basal-cell hyperplasia with minor nuclear abnormalities. (×320. Reduced one-sixth.)

B, Patient 15, NUMS No. 17584. Biopsy at 9 weeks post partum. Basal-cell hyperplasia with slight nuclear atypia. The smear was positive and the patient will be followed in spite of the cervical cautery necessary to control bleeding after biopsy. (×200. Reduced one-sixth.)



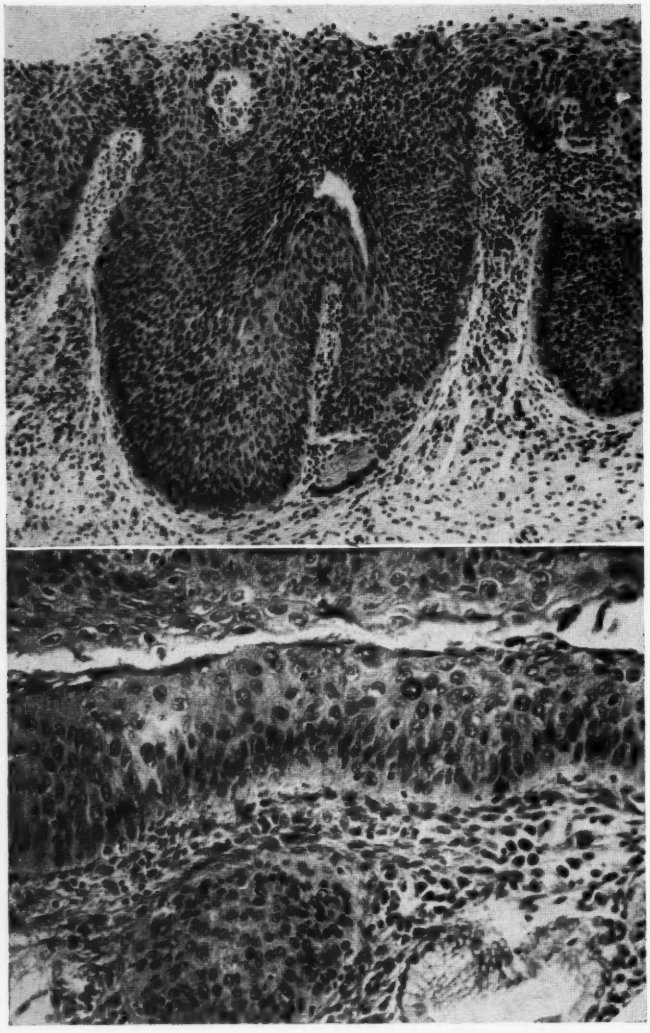
A. *B.*

Fig. 2.—*A*, Patient 16, NUMS No. 16825. Antepartum biopsy at 30 weeks. Preinvasive carcinoma of moderate differentiation. Normal architecture is lost, hyperchromatism is striking. (×360. Reduced one-sixth.)

B, Patient 16, NUMS No. 17902. Postpartum biopsy at 24 weeks. The epithelial abnormality has persisted. There is glandular extension in other areas. (×360. Reduced one-sixth.)

Though the criteria for the diagnosis of preinvasive carcinoma and the treatment of this lesion are not germane to this discussion, we share the opinion that these lesions, whatever you may choose to call them, are not transient

A.



B.

Fig. 3.—*A*, Patient 17, St. Luke's No. 2614-1951. Antepartum biopsy at 6 weeks. A lesion of mixed differentiation, poorly to moderately differentiated preinvasive carcinoma with glandular extension. (×120. Reduced one-sixth.)

B, Patient 17, NUMS No. 17027. Postpartum hysterectomy specimen at 37 weeks. Similar moderately differentiated lesion with glandular extension. (×200. Reduced one-sixth.)

Fig. 4.—*A*, Patient 18, NUMS No. 16668. Antepartum biopsy at 21 weeks. Detached epithelium with marked nuclear abnormalities but considerable differentiation in superficial layers. There is a marked cervicitis. Well-differentiated preinvasive carcinoma. (×290. Reduced one-sixth.)

B, Patient 18, NUMS No. 18024. Biopsy at 12 weeks post partum. Similar epithelial changes on the left extending into an endocervical gland. Opposing epithelium, though slightly tangentially sectioned, is relatively normal. (×100. Reduced one-sixth.)

C, Greater magnification of area outlined in Fig. 4,*B* to show moderately differentiated carcinoma. Abnormal mitotic figures (arrow) were common. (×320. Reduced one-sixth.)

D, A different area in the same biopsy (NUMS No. 18024). Somewhat better differentiation in superficial layers with early keratinization. (×220. Reduced one-sixth.)

E, Another area from the same biopsy (NUMS No. 18024). Nuclear abnormalities, though extending through the full thickness of the epithelium, are less striking; differentiation is more complete. The section is slightly tangential. (×110. Reduced one-sixth.)

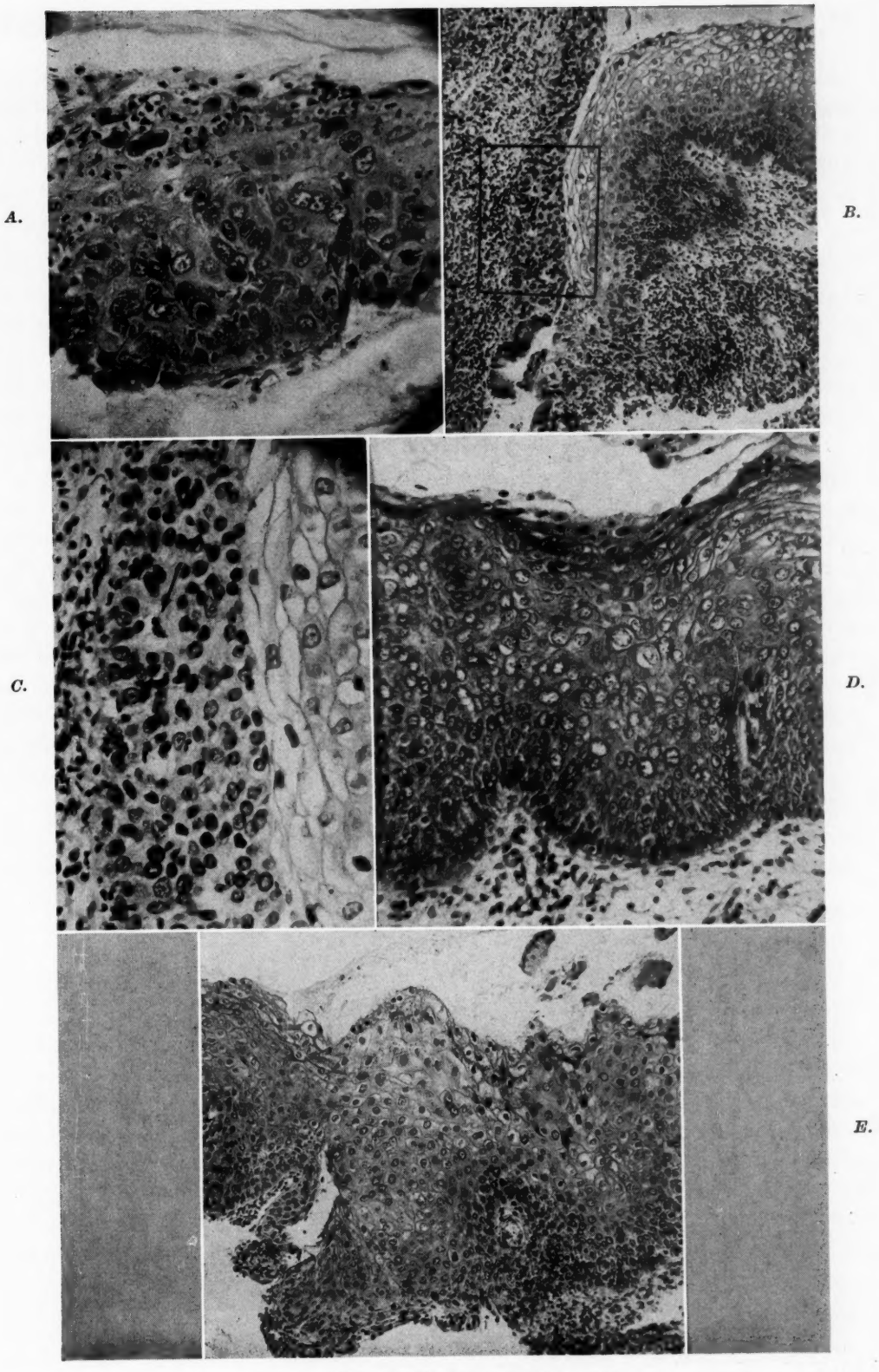
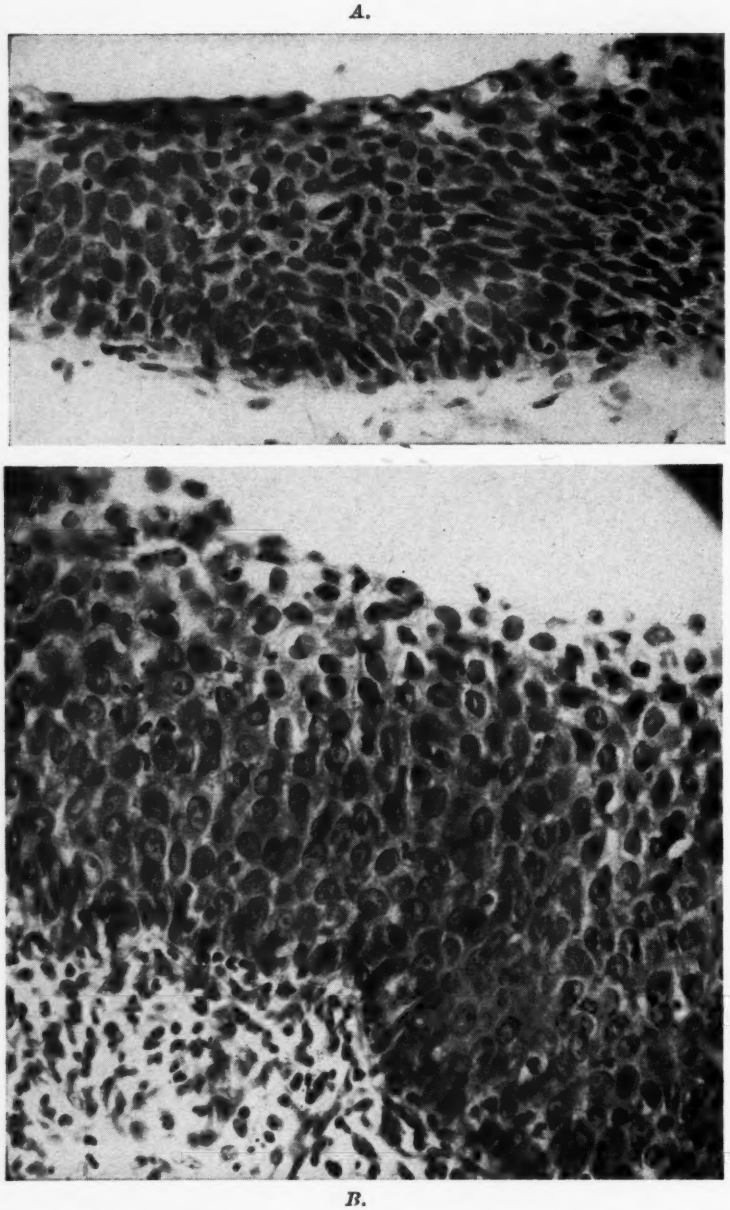


Fig. 4.—(*For legend, see opposite page.*)

"pregnancy changes," since most of them persist after the termination of pregnancy. To date, we have observed 19 such lesions in pregnancy. These lesions have been followed untreated through pregnancy and the immediate postpartum period. Observations on 14 of these lesions have been reported in detail elsewhere.[11] The details of the additional 5 are presented here.

These data have been obtained as a part of a larger study (in progress) concerning the cervix during pregnancy and the postpartum period. These



A.

B.

Fig. 5.—*A*, Patient 19, NUMS No. 17783. Antepartum biopsy at 24 weeks. Poorly differentiated preinvasive carcinoma. (×430. Reduced one-sixth.)

B, Patient 19, NUMS No. 17463. Hysterectomy specimen 8 weeks post partum. Lesion identical to that in Fig. 5,*A*. (×430. Reduced one-sixth.)

five lesions were found in biopsies of cervical abnormalities (eversion, laceration, etc.) or because of a previous abnormal smear. Three of these patients are from the Chicago Maternity Center. Two were private patients.*

We have chosen to depict rather than to attempt to describe these lesions. We consider them preinvasive carcinoma though some may disagree (there is at times disagreement even in our own laboratory, particularly with those lesions showing the greatest differentiation and the least nuclear atypia). However, the reader may make his own diagnosis, our major point being that, whatever you choose to call them, they cannot be "pregnancy changes" as they have persisted after pregnancy in most instances. Some have shown considerable variation in different areas (Fig. 4, *C, D, E*). The area considered most abnormal was, of course, selected wherever it was photographically possible.

Detailed data concerning each patient are presented in Table I. The number of quadrants biopsied in each instance is noted in parentheses. We believe adequate biopsies, adequate sampling of cone and hysterectomy specimens, immediate fixation and good tissue technicians are all important in such a study. We are particularly blessed in this latter regard.† In our laboratory four quadrant squamocolumnar junction biopsies are so prepared that 6 or 8 levels in each of the 4 biopsies are examined, additional sections being made as necessary. Cone and hysterectomy specimens are serially blocked and multiple sections cut from each block as necessary. We believe that these are important details if one is to avoid missing these lesions, some of which are minute.

Of the 5 lesions 4 have persisted (Figs. 2, 3, 4, and 5). In the fifth (Fig. 1, *A*) only a slightly atypical basal-cell hyperplasia was found on biopsy 9 weeks post partum (Fig. 1, *B*). Though the cervix was cauterized after this biopsy to control bleeding, the patient will be followed.

Comment

Of 19 lesions followed by us (14 in the previous report[11] and 5 presented here) 16, or 84.2 per cent, have persisted. Such lesions, therefore, can hardly be considered evanescent "pregnancy changes," nor can they be lightly dismissed as likely to disappear on termination of the pregnancy. We do not claim that the 3 lesions (or 15.8 per cent) that disappeared did so because they were completely removed by the biopsies. However, we do *not* believe that their disappearance (or rather our inability to find these lesions) can be credited to a purported, self-limited specific pregnancy change. A similar "disappearance" rate for such lesions is no doubt also found in most laboratories in *nonpregnant* patients. In our own laboratory no lesion was found in

*We are indebted to Dr. William Geittman, Chicago, and to Drs. Fred Brown and Carl S. Harper of Madison, Wis., for their permission to include their private patients, 17 (M. G.) and 19 (H. S.), respectively. We are also indebted to Dr. Edwin F. Hirsch, Pathologist, St. Luke's Hospital, Chicago, for allowing us to examine and photograph the biopsy specimen on patient 17 and for furnishing us tissue from the hysterectomy specimen from this patient. The diagnoses, however, are ours and we do not intend to imply that he necessarily agrees with them.

†Trained and supervised by Miss Mildred Milligan, Chief Technician, Laboratory of the Department of Obstetrics and Gynecology, Northwestern University Medical School, Chicago, Ill.

20.6 per cent of 138 hysterectomy or cone amputation specimens from patients (both pregnant and nonpregnant) in whom the diagnoses had previously been made by biopsy.[12] Discussion of the reasons for these real and/or apparent "disappearances" is not pertinent to this paper.

It is realized that a very few of the readers do not and will not accept the validity of the diagnosis of "preinvasive carcinoma." It is also realized that others may not accept the findings in one or more lesions depicted here, and previously,[11] as adequate for the diagnosis of preinvasive carcinoma. We hope that neither of these points of view will obscure the objective of this and our preceding publication on this subject, namely, that *these lesions discovered during pregnancy are not specific and evanescent pregnancy changes since the vast majority persist after the termination of the pregnancy.*

Summary

The details of 5 additional cases of preinvasive carcinoma of the cervix followed through pregnancy and the puerperium are presented. Four of the 5 persisted after the termination of pregnancy, being found in the biopsies and/or operative specimens. These cases added to the 14 previously reported (of which 12 persisted) make a total of 19 lesions of which 16, or 84.2 per cent, persisted. It is concluded, therefore, that, regardless of nomenclature, these abnormalities are not pregnancy changes.

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Discussion

DR. D. N. DANFORTH.—The excellent material upon which this paper is based is not easily obtained. I am interested to know the number of pregnant cervices which were biopsied in order to obtain the 19 cases which have been diagnosed as preinvasive carcinoma, and also whether there is any correlation with a gross lesion.

At the present time it is possible to make certain generalizations which are pertinent to the problem which these cases raise. First, in recent papers criteria have been established for the diagnosis of carcinoma in situ which appear now to be acceptable to most observers. For example, Te Linde requires for such a diagnosis that the individual cells, throughout the thickness of the epithelial layer, have the same characteristics as those of invasive cancer. If such a requirement is judiciously followed, there should be confusion only in the exceptional case. Second, evidence is accumulating which indicates that bona fide carcinoma in situ will ultimately be proved to be a progressive, irreversible lesion. If such a lesion is not destroyed or removed, it therefore can be reasonably predicted that it will, in an indefinite period, progress to invasive carcinoma. Third, there is

evidence that carcinoma in situ may have its origin at focal points in a field of basal-cell hyperplasia, and that the latter lesion, although it may be a precursor of carcinoma in situ, is nevertheless of itself strictly benign, and has definite transient or reversible possibilities. With respect to pregnancy, certain pertinent conclusions may also be made. First, it seems evident that there are no specific changes in the squamous epithelium which are peculiar to pregnancy. This fact has been repeatedly demonstrated by studies designed expressly to elucidate this point, and I believe at this moment is sufficiently established that some might take exception to the opening sentence of this evening's paper, which suggests that there is still wide divergence of opinion. Second, satisfactory evidence has now been recorded that there is an increased frequency of certain hyperactive changes during pregnancy, and that these changes, although not to be confused with true basal-cell hyperplasia, nevertheless quite definitely tend in that direction. These evidences of hyperactivity, although minimal, to be sure, are none the less definite, and are reversible.

How does this apply to the present work? This paper is an extension of two previous papers. The first of these demonstrated by cervical biopsies in pregnancy that there are no gestational changes which cannot also be found in the nonpregnant. The second, very recently published, presented 14 patients in whom preinvasive carcinoma of the cervix was diagnosed during pregnancy. In 12 of these a similar lesion was demonstrable after delivery. The present paper brings to 19 the number of cases diagnosed ante partum, of which 16 were evident after delivery. In the two latter papers it is emphasized, repeatedly, that although it is the authors' opinion that the 19 lesions were all carcinoma in situ, they are aware that not all will agree with the criteria which were used for making this diagnosis. Hence, they wish to omit this term from discussion, and to conclude only that they have found in 19 pregnant cervices a type of abnormality of the squamous epithelium which persisted after delivery in 84 per cent of the cases. I appreciate the reason for their reluctance, but believe it would be possible and desirable, without detracting from the work, to state with less hesitation the nature of the epithelial abnormality, and to label it conclusively as this or that pathological entity. Indeed, I do not think it possible to avoid considering this material in specific terms, since the paper presenting most of these data is entitled "Preinvasive Carcinoma of the Cervix in Pregnancy," and since all of the 19 lesions we now discuss were diagnosed preinvasive carcinoma. Furthermore, when the authors state in both papers that their criteria for diagnosing carcinoma in situ are not uniformly acceptable, I believe that they are obliged to record specifically the criteria which they have used, and discuss these lesions in such terms. Without this information I believe it difficult to evaluate this material.

With respect to the particular areas which are illustrated, I am sure that they have no relation to my own conception of the ordinary, minimal hyperactive changes which one might properly expect upon minute study of the normal cervix in pregnancy, and I believe that others will agree. If they are true preinvasive carcinoma they should of course persist, as occurred in 16 of the 19 cases. But if they were true basal-cell hyperplasia they might also persist. One other possibility might be mentioned: if the authors believe that the lesions fall short of the most rigid criteria for carcinoma, yet persist after pregnancy, is it possible that they may represent a type of "pregnancy change" or "pregnancy reaction" which is *not* reversible, and which has not been heretofore described? I should appreciate Dr. Peckham's thoughts on this.

What of the lesions which vanished? This point, which the authors consider irrelevant at this time, I believe is also very pertinent. Why do we find such frequent reports of the magical disappearance of preinvasive carcinoma in pregnancy, when, for the nonpregnant, ordinary natural laws usually provide a satisfactory explanation? On the basis of the evidence available to date, it is logical to conclude either that the lesion was entirely removed by the original biopsy, or destroyed by cauterization, or missed in subsequent search for it; or it was not a true carcinoma in situ in the first place. It is necessary that one of these explanations be applied to each of the 3 lesions which disappeared. With respect to pregnancy, it seems reasonable that the inherent tendency to hyperplasia which is present at this time may modify pre-existing epithelial abnormalities which are

unrelated to the pregnancy. Hence, as suggested in the first of the three papers cited, one may expect greater confusion in the interpretation of these lesions in the pregnant than in the nonpregnant. However, when all this information is assembled we appear to be left with the fact that when the absolute criteria for preinvasive carcinoma are present, one must make this diagnosis irrespective of pregnancy. And when this diagnosis is made, one should expect the course which the authors found in 16 of their 19 cases.

DR. JOHN I. BREWER.—It is not the purpose of this paper to discuss or to argue that the lesions shown are or are not carcinoma in situ. The lesions are presented as epithelial changes in the cervices of pregnant women which persisted after pregnancy. They are identical to changes in the cervices of nonpregnant women. They disappear spontaneously with approximately the same degree of frequency. They are identical to so-called carcinoma in situ in the nonpregnant tissues.

They are not like the minimal changes described by Danforth and are not to be confused with them. The latter were not suggestive of carcinoma in situ or of basal-cell hyperplasia. Danforth did not consider them as carcinoma in situ but his statement which I quote, "Since the deviations noted in pregnancy are hyperactive ones, it is suggested that during pregnancy one's attitude toward equivocal or borderline cervical cancers should be particularly conservative," has induced some authors to claim and to quote the work as proof that epithelial changes in the cervix during pregnancy might simulate carcinoma in situ.

The paper tonight with the adequate follow-up of patients and material indicates this is not true and that the extensive changes observed are not dependent upon the pregnancy state but rather are changes that can occur and persist in any cervix, whether the patient is or is not pregnant. It now seems clear that such lesions are true ones, are not an integral part of pregnancy, and should be treated as such.

DR. R. R. GREENE.—I, also, would like to comment on the remarks by Dr. Danforth. To him everything pertaining to this subject is apparently very clear and simple. To us it is not. Dr. Danforth said that good evidence is accumulating that preinvasive carcinoma necessarily terminates in invasive carcinoma. Actually, that is not true, much as we all believe it. There is good evidence that many invasive carcinomas have been preceded by preinvasive carcinoma by five or ten years. There is, however, no good evidence yet that the preinvasive lesion necessarily terminates as an invasive carcinoma. No one has reported a series of patients on whom a diagnosis of preinvasive carcinoma was made and then determined what percentage of those patients ended up with invasive carcinoma. Obviously, with the slow progress of this lesion, it is going to be ten or fifteen years before it is shown that this always happens.

Dr. Danforth's remarks about the accepted, clear-cut criteria for the diagnosis of preinvasive carcinoma are fine in theory but not always in practice. Unfortunately, there is an occasional lesion that is most difficult to diagnose. This is particularly true of the well-differentiated lesion in which the nuclei while still abnormal tend to mature as they near the surface. This causes a lack of uniformity in the different layers of the epithelium. Because of this lack of uniformity, some observers will not make the diagnosis of preinvasive carcinoma with such a lesion.

Dr. Danforth quoted us as being aware that not all will agree with the criteria which we use in making the diagnoses. His implication is that this refers to all of the lesions. This is distinctly not true. The vast majority of the lesions, as depicted here tonight and in our previous publication on the subject, are clear cut, unequivocal, so-called preinvasive carcinomas of the cervix. I am sure such a diagnosis would be acceptable to almost anyone competent to render the diagnosis. A few of the lesions were of the well-differentiated variety previously mentioned. Whether they are or are not true preinvasive carcinomas is irrelevant. The point we have been trying to make tonight and in the previous publications is that these abnormalities are not evanescent pregnancy changes since they persist long after the termination of the pregnancy.

Dr. Danforth showed distress that we did not give in detail our criteria for the diagnosis of preinvasive carcinoma of the cervix. This was done in our previous publication on this subject. We did not think it was necessary to repeat it.

DR. EUGENE A. EDWARDS.—I wish to ask a couple of questions. I have been in the practice of gynecology and obstetrics for years and I have never seen one mature carcinoma of the cervix in a pregnant woman. I do not believe that we very often see carcinoma of the cervix in 20-year-old women. I just wonder, although these pictures were beautiful and looked like carcinoma of the cervix, how many were clinically carcinomas. I wonder how many of the older group in this organization have seen carcinoma of the cervix in a 20-year-old woman. Maybe once or twice in a lifetime. As I understand it, in this paper there were two or three women of 20 years on whom a hysterectomy was performed. What would have been their course if not operated upon? I think there is another side to this problem besides the microscopic side. There is also a clinical side.

DR. BEN M. PECKHAM (Closing).—Dr. Danforth's discussion has been rather adequately discussed. There are just a few points that I would like to mention that were not considered by Dr. Brewer or Dr. Greene. He mentioned our material. Actually, we have examined 500 biopsies from pregnant and immediately postpartum patients (350 and 150, respectively). This can have nothing to do with the incidence of these lesions in pregnancy because it is a highly selected group. Most of them were obtained from patients with abnormal cervices or abnormal smears selected from an unknown number of patients seen in the last 5 or 6 years at the Chicago Maternity Center, Northwestern Clinics, and in the private practices of many who have sent us material from all over Chicago and cities in the Middle West. If I may hazard a guess at this total number, probably somewhat in excess of 10,000 to 15,000 patients.

I think the remarks about divergence of opinion not being present, and about the need for such a study have been adequately covered.

We are sorry that Dr. Danforth had difficulty in evaluating the lesion from the photographs. The reason we presented so many photographs in this paper is that we think they more clearly represent what we are talking about than any lengthy description. One may read pages of description and still wonder exactly what the writer is talking about. One would rarely make a diagnosis on the basis of a single photomicrograph, but one would be even less likely to do so on the basis of written description.

Dr. Danforth made the remark that if these lesions were true basal-cell hyperplasia, they might also persist. If he means by true basal-cell hyperplasia what we mean by atypical basal-cell hyperplasia, it is true that many do persist. We have been able to follow a number of such lesser lesions through one or more pregnancies. This will be the subject of another communication. As to the tendency of pregnancy to modify atypical basal-cell hyperplasia to the point where it could be confused with preinvasive carcinoma—if this occurs, we have not noted it.

Dr. Danforth asks whether these lesions might not be an irreversible "pregnancy change" which has not heretofore been described. I think this is another way of asking me whether pregnancy causes preinvasive carcinoma. If so, I don't know the answer to this question.

INVESTIGATIONS ON THE USE OF SODIUM-REMOVING RESINS IN THE TREATMENT OF PRE-ECLAMPSIA*†

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DIETARY sodium deprivation is a well-established principle in the treatment of pre-eclampsia. Indeed, this principle of therapy has been extended, and it is often employed early in pregnancy to avert sodium and water retention in an attempt to prevent the development of pre-eclampsia.[1] The simplest method of reducing the sodium content of the body is, of course, by dietary means designed to restrict the intake of salt. A rigid low-salt diet requires careful supervision, is unpalatable to most patients, and is rather inefficient in the treatment of pre-eclampsia. A more rapid reduction of body sodium could be expected when a low-salt diet is combined with diuretic agents. Unfortunately, the most effective diuretic agents are not without danger when administered to pre-eclamptic patients and, as a result, are infrequently employed.

It has been demonstrated conclusively that ion exchange resins will remove cations from enteric fluids after the oral ingestion of such resins and, when combined with a restricted sodium diet, will eventually produce a negative sodium balance.[2, 3] Extensive studies on a variety of clinical states in which mobilization of edema fluid appeared to be desirable have led to the accumulation of a large body of experimental data.[4, 5, 6]

The possibility that exchange resins might prove to be an adjunct in the treatment of water retention of toxemic patients has been considered by a number of investigators. Recent publications by Odell, Janssen, Novelli, and Ralston,[7] Penman,[8, 9] and Carey[10, 11] relate their experiences in the use of these resins in various types of pathologic pregnancies with rather divergent results.

The studies presented here were planned and directed (1) to determine whether the ingestion of sodium-removing resins in the presence of a low-salt diet would lead to a negative sodium balance in pre-eclamptic patients, (2) to determine the extent and consequences of changes in electrolyte and water metabolism produced by this regime, (3) to establish the effect of this therapy on the clinical course of toxemic patients; to prevent, if possible, a premature termination of pregnancy in severe pre-eclampsia, and (4) to devise a simple, safe, and effective plan for the administration of cation exchange resins in the treatment of pre-eclamptic patients.

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†The deuterium oxide used in this investigation was a gift of the Ortho Research Foundation, Raritan, N. J.

Clinical Material

Four patients were studied in an attempt to document the quantitative changes in body electrolytes and water metabolism resulting from the ingestion of therapeutic amounts of resins. The effect, if any, on the prolongation of pregnancy or other symptomatic improvement was considered trivial and incidental for this series. A fifth patient, E. D., was included in order to postpone, if possible, the termination of pregnancy until at least the thirty-sixth week of gestation. This prolongation in the period of gestation was to be allowed if no progression of the existing manifestations of pre-eclampsia became evident. Studies on a sixth and a seventh patient provide data which, based upon the information obtained from the preceding group, illustrate a routine clinical application of resin therapy with the minimum of laboratory data compatible with the safe and effective administration of resin.

In order to provide a basis for comparison the first group has been fitted into a uniform pattern of study. These patients were closely supervised in the antepartum clinic and had received the usual ambulatory treatment for pre-eclampsia for varying periods of time prior to hospitalization. This ambulatory treatment consisted of restricted activity, low-salt diet, mild sedation, and ammonium chloride as directed by the resident physician and the attending medical adviser. The patients were hospitalized when a progression of two or more of the cardinal signs of pre-eclampsia became apparent.

On admission to the hospital, the patients were placed on a period of control lasting two to four days. This consisted of bed rest, a low-salt diet without water restriction, and mild sedation. Control values collected during this time included "deuterium oxide space," water turnover rate, "sodium space," total body sodium, blood volume, serum carbon dioxide combining power, serum uric acid, serum nonprotein nitrogen, serum protein, urinary sodium output, quantitative urinary output of protein and quantitative sodium intake.

After the control period, the patients were given the maximum tolerated dose of Carbo-Resin,* usually about 72 Gm. per day, in three divided doses. When the urinary sodium output and the serum carbon dioxide combining power started to decrease, determinations of deuterium oxide space, sodium space, and blood volume were repeated. The resin was then discontinued and the patient allowed to return to the course as defined for the control period. After an interval of from 3 to 7 days, these determinations were repeated in order to establish changes which might have resulted from cessation of therapy.

These data are reproduced in graphic form in Figs. 1 to 4. A brief clinical history is given for each patient together with a discussion of significant events which occurred during the period of investigation. The clinical course of Patient 5 is depicted graphically in Fig. 5; therapy in this case was specifically directed toward control of the existing manifestations of pre-eclampsia and

*The exchange resin, Carbo-Resin, used in this study was contributed by Eli Lilly and Company, Indianapolis, Ind. This material is an unflavored powder consisting of 12 parts alkylene polyamine resin, 29 parts of the potassium salt of carboxylic acid resin, and 59 parts of the carboxylic acid resin.

prolongation of the period of gestation in order to increase the maturity of the fetus. The presentation of the data on the sixth and seventh patients is restricted to a brief summary of their clinical courses.

Methods

A. Sodium Space and Total Body Sodium.—The method of Kaltreider and co-workers[14] had to be modified because of the need of repeated determinations on the same patient. A maximum dosage of 30 microcuries of Na^{24} was used per determination.

The radiosodium, in the form of isotonic chloride, was administered by infusion from a calibrated analytic burette. Serum samples at 3, 5, and 24 hours were obtained and their radioactivity determined. An aliquot of the 24 hour urine sample was used for flame-photometric determination of sodium as well as an estimation of its radioactivity. For the counting procedure, 0.5 c.c. of serum and 2.0 c.c. of urine were placed in sample pans and heat dried under an infrared lamp. The relatively low activity of all these samples necessitated the use of a Q-gas counter to achieve sufficient accuracy and precision. The sodium space and total body sodium were then calculated according to the following formulas:

$$\text{Total Body Sodium} = \frac{(\text{Amounts of } Na^{24} \text{ in counts/min. injected} - \text{Amounts of } Na^{24} \text{ in counts/min. excreted})}{\frac{\text{Concentration of } Na^{24} \text{ in Plasma in c./min.}}{\text{Concentration of Na in Plasma in meq./c.c.}}}$$

For purposes of a rough comparison this is identical with

$$\text{Total Body Sodium} = (\text{Sodium Space}) \times (\text{Concentration of } Na^{+} \text{ in Plasma})$$

B. Deuterium Oxide Space and Deuterium Oxide Turnover Rate.—The term "deuterium oxide space" is used interchangeably with the term "total body water." For its determination, a known volume of 99.8 per cent deuterium oxide containing 0.85 per cent sodium chloride, usually 40 to 50 c.c., was administered from a calibrated analytic burette and samples of blood withdrawn after equilibrium had been established.[12] The deuterium oxide concentration in the serum was determined by the "falling drop" procedure, and the total body water was calculated according to the formulas previously reported.[12, 13]

Incidental samples of serum collected during the period of investigation were used to determine the average turnover of water per day. For the calculation of this turnover constant, it is necessary and sufficient to define two points on the disappearance curve. The constant, which is proportional to the turnover, can then be calculated from the exponential equation:

$$A_t = A_o\, e^{-kt}$$

where A_t represents the concentration of deuterium oxide at time (t), A_o the equilibrium concentration of deuterium oxide, and k the disappearance constant. The data obtained by these calculations represent average values only, since strict regulation of water intake and output was not attempted.

C. Blood Volume Determination.—A modification of the dye dilution method described by Plentl and Gelfand[15] was employed. Three to 4 mg. of Evans blue (T-1824) was used for each determination in order to avoid excessive discoloration of the patient's skin and scleras. The concentration of the dye was then determined by means of a Beckman Spectrophotometer at 620 mμ by the usual technique.

D. Other Methods.—Serum sodium and potassium as well as the total urinary sodium output were estimated by the flame-photometric technique. Serum carbon dioxide combining power, serum nonprotein nitrogen, serum uric acid, and serum protein and chloride were determined by the usual standard laboratory procedures. Urinary protein was determined by the Esbach method using aliquots of 24 hour pooled urine.

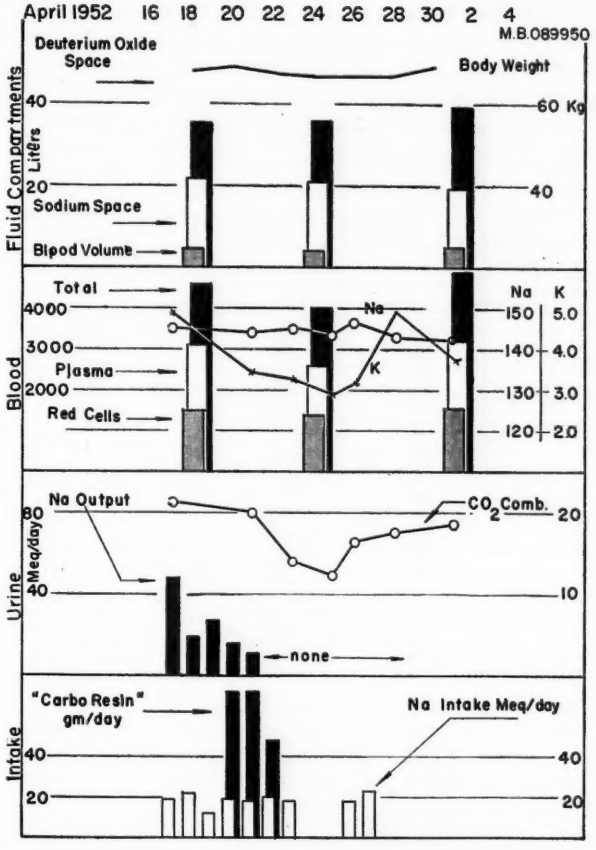

Fig. 1.—Graphic presentation of laboratory data obtained on patient M. B. near term.

Case Reports

Case 1.—M. B. (089950) (Fig. 1) was a 31-year-old gravida vi, para i, who was under private care during the first portion of her pregnancy. Her blood group was A, the Rh factor negative; the Coombs test remained negative throughout her pregnancy. Beginning at the thirtieth week she gained weight rapidly. This reached a maximum during the thirty-fourth week at which time the blood pressure was 142/92. The reflexes became hyperactive but there was no albumin in the urine.

Her private physician prescribed Carbo-Resin, 24 Gm. three times a day while she was ambulatory, but since this therapy was thought to be still in the experimental stage, closer supervision in the hospital was advised. On the day following admission to the hospital, a determination of the fluid compartments, blood constituents and urinary sodium was made. The blood uric acid was 3.5 mg. per 100 c.c., the nonprotein nitrogen 30.7 mg. per 100 c.c. After a control period of three days the patient received Carbo-Resin, in the usual dosage. The urinary sodium output, serum sodium, and plasma volume decreased progressively during the period of therapy. On the second day of therapy the patient's urinary sodium

output dropped to zero, and the carbon dioxide combining power was 13 meq. per 100 c.c. The determination of fluid compartments was repeated, and it was found that in the presence of a moderate loss of weight the percentile changes in total body water and sodium space were negligible. Although the patient received no further therapy, the urinary sodium output remained close to zero, until termination of the pregnancy five days following her discharge from the hospital. Serum sodium and carbon dioxide combining power returned to normal levels within a few days indicating that sodium depletion had not been carried to extreme proportions. Simultaneously with the establishment of a normal acid-base balance, the patient showed a slight increase in weight and a corresponding increase in total body water. Following her discharge, she continued to gain weight and was readmitted four days later with the signs and symptoms of premature separation of the normally implanted placenta. She was delivered of a premature baby by cesarean section.

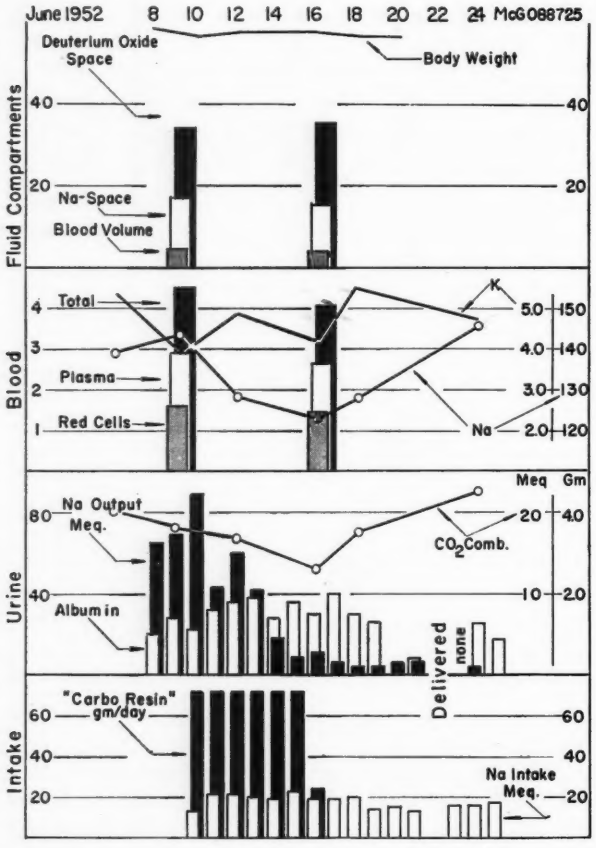

Fig. 2.—Graphic presentation of laboratory data obtained on patient McG. The urinary albumin output is given in grams per 24 hours, its scale is shown on the right.

CASE 2.—McG. (088725) (Fig. 2) was a 25-year-old primigravida who was first seen in the antepartum clinic during the twenty-fourth week of gestation. The past history and the systemic review were noncontributory; the pelvis was typed as gynecoid and the blood pressure was found to be 120/82. At the second antepartum visit, during the twenty-ninth week of gestation, 2 plus ankle edema was noted but the remainder of the examination was negative. She was given another appointment for the thirty-first week, at which time the blood pressure had risen to 154/94; a urine analysis showed the presence of 4 plus albumin and she had pronounced facial and ankle edema. The reflexes were markedly hyperactive,

and the ocular fundi showed focal constriction of arterioles with minimal tortuosity. The uric acid concentration of the serum was 6.4 mg. per 100 c.c. The blood count was within normal limits. Following admission to the ward she was placed on bed rest and sedated with morphine sulfate.

On the third day following her admission, the study was begun with the determination of the control values. During the control period all blood chemical values and sodium output were within normal limits. The total body water amounted to 59 per cent and the sodium space to 29 per cent of the total body weight. Following the institution of therapy, which consisted of 72 Gm. of sodium-removing resin per day, there was a persistent drop in urinary sodium output, a decline in carbon dioxide combining power, and a drop in serum sodium. When the carbon dioxide combining power and the serum sodium concentration had reached their lowest value, and the daily urinary sodium output had dropped to less than 5 meq., resin therapy was discontinued. The determination of fluid compartments was then repeated. The total body water had decreased to 57 per cent of body weight, while the sodium space had decreased to 27 per cent of body weight.

Although no further sodium-removing resin was administered, the daily urinary sodium output remained below 5 meq., indicating a sodium depletion of a pronounced degree. This retention of sodium was obviously necessary in order to correct the compensated acidosis as shown by the subsequent rise in the carbon dioxide combining power and serum sodium. A moderate rise in serum potassium at this point might be interpreted as indicating a "shift."

Throughout the whole period of study, the patient continued to spill albumin to a measurable degree at a maximum rate of 2.0 Gm. per day. There was no appreciable change in albuminuria during the period of study.

She went into labor spontaneously during the thirty-fourth week of gestation, and was delivered of a 1,720 gram baby nine hours later. Her postpartum course was unremarkable. When seen one month after discharge from the hospital, her blood pressure was 108/70 and the urine was free of albumin. Three months later her blood pressure was 120/78.

CASE 3.—M. R. (982385) (Fig. 3) was a 23-year-old primigravida who was first seen in the antepartum clinic in the fourteenth week of gestation. She had an average gynecoid pelvis, the blood group was A, the Rh factor positive, and the serologic test for syphilis was negative. Her past history and systemic review were noncontributory. An analysis of the urine was within normal limits. The blood pressure was 118/80. She had an uneventful antepartum course until the thirty-fourth week, when the blood pressure rose suddenly to 142/96. This was associated with rapid weight gain and albuminuria.

Following admission to the ward she was placed on bed rest and routine sedation. She was subjected to the usual control period when the basic values for fluid compartments, blood, and electrolyte concentrations were determined. The total body water was found to constitute 54.8 per cent of the body weight, and the sodium space 37.9 per cent. Following the administration of sodium-removing resin, the urinary sodium output began to decrease. A decline in the carbon dioxide combining power indicated a state of compensated acidosis. On the fifth day following the institution of resin therapy, the total body water had decreased to 52.9 per cent of body weight, and this decline was associated with a reduction in sodium space to 26.3 per cent. Unfortunately, the patient did not cooperate further and refused to take additional resin. The daily urinary sodium output then began to rise to inexplicable heights, which gave rise to the suspicion that the patient obtained sodium chloride from outside sources. Upon the cessation of resin therapy the carbon dioxide combining power began to rise, as did the serum sodium. There was a minimal gain in weight with minimal increase in total body water, but a considerable rise in sodium space. During the second period of the experiment there must have been a shift of water from the intracellular to extracellular fluid compartments which is further substantiated by a rise in serum sodium and fall in serum potassium during that period.

At the end of the experimental period the patient was discharged in improved condition, only to return in active labor two days later. She had a normal spontaneous delivery

of viable, premature twins. Deuterium oxide space and blood volume determinations were repeated on the fourth postpartum day. The postpartum course was normal. The blood pressure one month after delivery was 128/80.

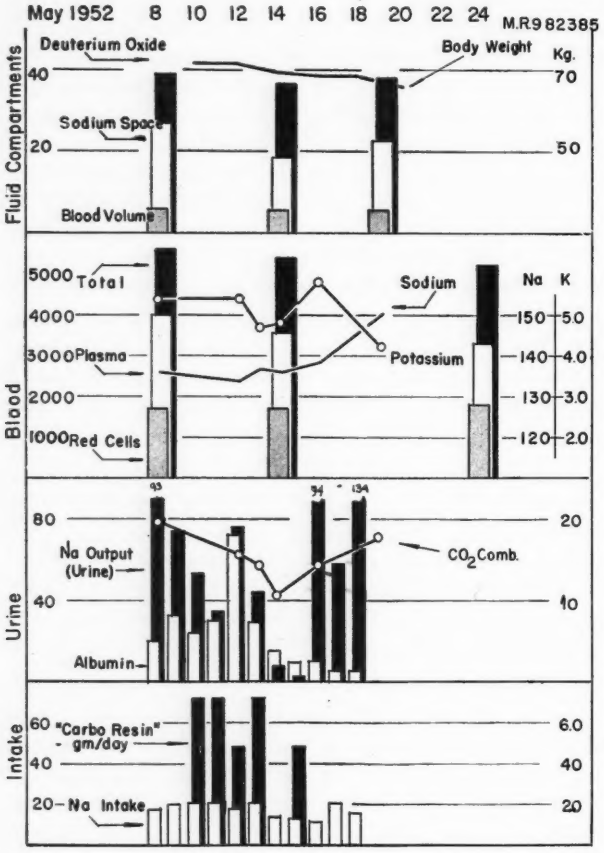

Fig. 3.—Graphic presentation of laboratory data obtained on patient M. R. near term. The urinary albumin output is presented in the same manner as in Fig. 2.

CASE 4.—M. W. (961260) (Fig. 4) was a 26-year-old gravida iii, para ii, who was first seen in the antepartum clinic during the thirty-third week of gestation. She had a documented history of hypertensive cardiovascular disease for eight years prior to her present pregnancy, and both previous pregnancies were associated with severe pre-eclampsia. On physical examination the significant findings were moderate pretibial edema and a blood pressure of 190/140; routine urine analysis showed 3 plus albuminuria.

The patient was immediately admitted to the ward, because it was felt that she was subject to imminent convulsions. On the day following admission the routine determinations of body fluid compartments and electrolytes were performed. In addition to the data presented in graphic form in Fig. 4, the blood uric acid was 4.2 mg. per 100 c.c., and the nonprotein nitrogen was 27.3 mg. per 100 c.c. A routine blood count was within normal limits, and a quantitative determination of albumin for the first 24 hour period showed the presence of less than 0.2 Gm. per liter.

Following a 3 day control period, the patient was placed on Carbo-Resin therapy as a result of which the usual drop in urinary sodium output occurred. There was also a drop in total body water from 54.5 per cent to 50.3 per cent of total body weight, as well as a decline in sodium space from 34.7 to 22.9 per cent of total body weight during that period.

The carbon dioxide combining power, in contrast to that of the other patients investigated during this study, did not decrease. Although there was a moderate drop in the serum sodium concentration, this patient did not show the expected degree of compensated metabolic acidosis. All determinations of fluid compartments were repeated three days later and there was no significant change in sodium space or total body water. Albuminuria was less than 0.5 Gm. per day throughout the experimental period, and did not change as a result of treatment.

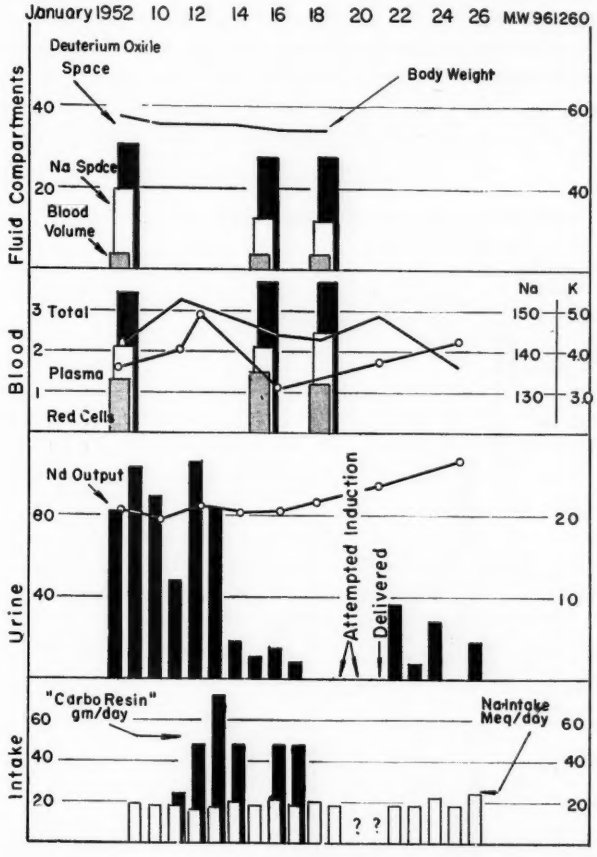

Fig. 4.—Graphic presentation of laboratory data obtained on patient M. W. near term.

Since the termination of pregnancy was thought to be imperative, Pitocin inductions were attempted on two successive days. A third attempt was not necessary because the patient went into labor spontaneously after rupture of the membranes. She had an uncomplicated labor and was delivered of a 2,070 gram baby. The postpartum course was uneventful. A tubal ligation was performed on the eighth postpartum day, and she was discharged in good condition on the eleventh postoperative day. When seen six weeks after discharge from the hospital, her blood pressure was 170/110. One year post partum, her blood pressure was 180/130 and there was moderate albuminuria.

Case 5.—E. D. (999128) (Fig. 5) was a 24-year-old multipara, whose first pregnancy terminated in a complete abortion at 10 weeks' gestation. Her second pregnancy was uneventful until the thirty-fifth week when the blood pressure rose to 170/120, coincident with the onset of albuminuria and generalized edema. She was delivered of a premature baby by cesarean section because she failed to respond to "therapy."

For her present pregnancy she registered during the sixth week of gestation. The blood pressure was slightly elevated (142/96), and her initial weight was 73.2 kilograms.

She was placed on a low-calorie, low-salt diet and did well until the beginning of the thirty-first week, when the blood pressure began to rise and she developed 4 plus albuminuria. She was, therefore, admitted to the hospital where her initial therapy consisted of sedation. This was supplemented by the administration of Carbo-Resin after the usual control studies were completed. The course and the changes in fluid compartments and electrolytes are presented in graphic form in Fig. 5. The significant developments in the therapy of this patient were (a) a prolonged response in terms of decreased urinary sodium output to relatively small amounts of resin, (b) the persistent reflection of the carbon dioxide combining power as an index of the effectiveness of therapy, and (c) a striking decrease in albuminuria during the course of treatment. Under this regime her pregnancy was carried to the thirty-sixth week of gestation. Following the spontaneous onset of labor, a secondary cesarean section was performed and the patient delivered of a 1,955 gram baby. Her postoperative course was uneventful.

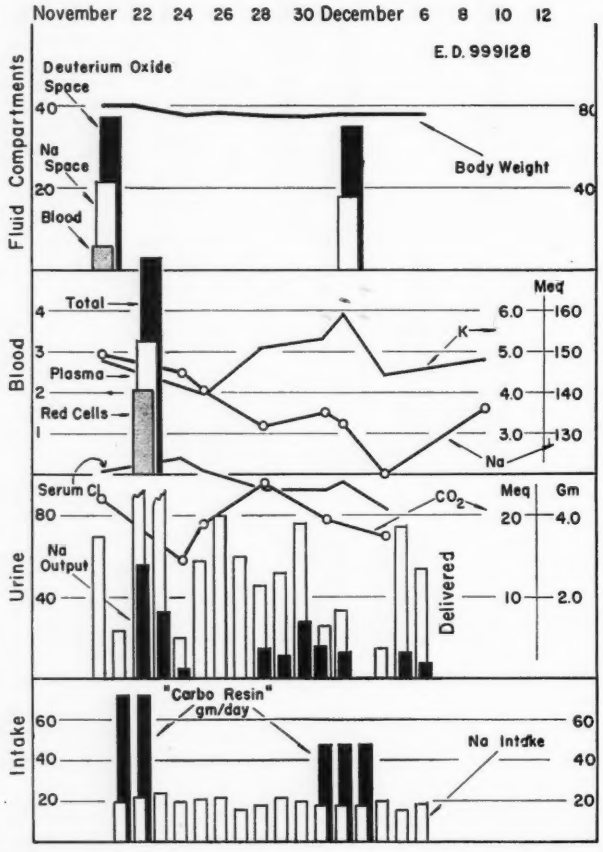

Fig. 5.—Graphic presentation of laboratory data obtained on patient E. D. near term. The urinary albumin output is presented in the same manner as in Fig. 2.

CASE 6.—I. R. (094722) was a 20-year-old gravida ii, para o, who was first seen in the antepartum clinic during the twenty-sixth week of gestation. Her past history and the systemic review were noncontributory. Her first admission to the hospital occurred during the thirty-first week because of a 14 pound weight gain within the preceding four weeks, associated with moderate albuminuria, 1 plus edema of all extremities, and a rise in blood pressure to 130/94. The control studies revealed a carbon dioxide combining power of 20.5 meq. per liter, serum sodium of 143.7 meq. per liter and serum potassium of 4.7 meq. per liter. She received small amounts of phenobarbital and 215 Gm. of sodium-removing resins over

the following three days. This produced a considerable weight loss and an appreciable decrease in hypertension. The urinary sodium excretion was nearly zero on the fourth day of therapy. She was then discharged from the hospital and placed on a 1,500 calorie salt-poor diet.

One week later, she was again hospitalized because of 3 plus albuminuria, 1 plus edema of all extremities, a rise in blood pressure to 176/110, and a weight gain of 10 pounds. On admission her blood pressure was found to be 150/102, the carbon dioxide combining power 18.8 meq. per liter, the sodium 143.5 meq. per liter, and the serum potassium 4.5 meq. per liter. She was again placed on oral Carbo-Resin and received 216 Gm. in three days. This was followed by an 8 pound weight loss and a reduction in urinary sodium output.

She went into labor during the thirty-fifth week, and had a spontaneous delivery of a normal 1,975 gram infant. The postpartum course was marked by a low-grade fever, attributable to pyelitis which responded to chemotherapy.

CASE 7.—A. I. (925966) was a 25-year-old gravida vi, para ii, who registered during the nineteenth week of gestation. Four of her previous pregnancies had resulted in spontaneous abortions. The other pregnancies were complicated by severe pre-eclampsia, culminating in the delivery of two premature infants. From the nineteenth to the thirty-second week she gained 11 pounds and had an entirely normal course but then developed generalized edema, without proteinuria, hyperreflexia, or hypertension. In view of her previous history of pre-eclampsia, she was immediately admitted to the hospital. At the time of her admission, the concentration of significant blood constituents was as follows: uric acid 4.3 mg. per 100 c.c., nonprotein nitrogen 48.4 mg. per 100 c.c., and a carbon dioxide combining power of 21.0 meq. per liter.

The 24 hour urinary sodium output for the first hospital day was 39.4 meq. She received 60 Gm. of Carbo-Resin per day for three successive days. The sodium output dropped to zero on the fourth day of resin therapy, coincident with a decrease in sodium output and a decline in carbon dioxide combining power to 17.6 meq. per liter. Since the edema had disappeared resin therapy was discontinued, and the patient discharged on a low-salt diet.

She was followed at weekly intervals until term. No progression of signs and symptoms of pre-eclampsia was noted. She had a spontaneous delivery of a 3,165 gram normal infant.

Comment

The clinical usefulness of cation exchange resins has been investigated most extensively in the field of internal medicine.[4, 5, 6] It seems likely that such therapy would prove useful in the management of all types of water and sodium retention, including that of the toxemias of pregnancy. The published reports on this subject are few.

Odell, Janssen, Novelli, and Ralston[7] found that the daily administration of 45 Gm. of a mixed resin, combined with a low-salt diet, when continued for about five days, resulted in a significant weight loss in a series of pre-eclamptic patients. These authors placed great emphasis on the finding that pituitrin is less effective in its hypertensive action when administered to patients so treated. Penman[8, 9] administered a daily dose of 45 Gm. of a potassium and ammonium polycarboxylic acid resin to a series of ambulatory patients. The effectiveness of the resin was evaluated by a loss of edema and a decrease in body weight. He concluded that resin therapy was a valuable adjunct in the treatment of pre-eclampsia.

In contrast to these investigators, Carey[10, 11] placed considerably less emphasis upon changes in body weight but stressed demonstrable changes in body

sodium for the evaluation of the effectiveness of the resin. He concluded that sodium-removing resins, when administered in adequate dosage and associated with a low-sodium diet and high fluid intake, reduced edema more rapidly than other routine methods of treatment. He further suggested that such therapy may be of value in prolonging pregnancies in certain pre-eclamptic patients.

For an analysis of the present data it seems most advantageous to discuss laboratory and clinical data successively and to coordinate them in a final summary. The most striking and consistent observation, which is also the most significant, is the drop in urinary sodium output per 24 hours following the ingestion of therapeutic amounts of Carbo-Resin. The initial urinary sodium output during the control period of our patients ranged from 40 meq. to a maximum of 105 meq. per 24 hours.

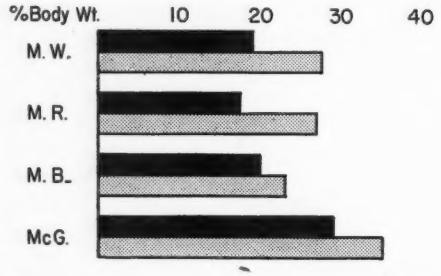

Fig. 6.—Changes in the "intracellular fluid compartment" (D_2O space minus Na^{24} space) before and after treatment with Carbo-Resin. The solid blocks represent control values, the stippled blocks the values obtained at maximal sodium retention.

A few days after the initiation of resin therapy, there was a drop to less than 5 meq. per 24 hours in all patients. This phenomenon is interpreted to be a maximum conservation of base by the kidneys in response to the fecal loss of sodium. Such a conservation appears to be necessary in order to compensate for the metabolic acidosis produced by the removal of large amounts of cations.

Subjects 1 to 5 showed a consistent and marked reduction in the "sodium space," which amounted to a maximal loss of 40 per cent in one patient. Although there was a concomitant drop in total body water as determined by the dilution of deuterium oxide, the percentile changes of the two compartments seem to be significantly different. Total body water decreased roughly in proportion to body weight and the decline in "sodium space" exceeded the decrease in body water relatively and absolutely.

Although the "sodium space" is known to exceed the extracellular space because of the presence of sodium ions within the cell and solid deposits of sodium, it may be taken as a measure of extracellular volume provided certain reservations are kept in mind. A shift of potassium from intracellular fluid to extracellular fluid may occur in order to compensate for the decrease in concentration of sodium. Since the concentration of potassium in serum remained constant during the experimental period, one may assume that the potassium-sodium-shift did not occur, or its contribution to the decrease in "sodium space" was negligible. The proportionately greater decrease in sodium

space over the decrease in total body water could then be interpreted as an absolute increase in the intracellular compartment. The magnitude of these changes is illustrated in Fig. 6, where the control values for the "intracellular fluid space" (deuterium oxide space minus sodium space) are compared to the corresponding figures at maximal retention, i.e., at the height of metabolic acidosis.

The changes in the relative and absolute sodium content before and after therapy are illustrated in Table I. The most significant values reported in that table appear to be those relating to milliequivalents per kilogram of body weight. During the control period these values seem to be extraordinarily high compared to figures reported for the nonpregnant normal woman. Further interpretation of these data will have to be postponed until the completion of studies on sodium space and total body sodium during uncomplicated pregnancies. These studies are now in progress and are nearly complete.

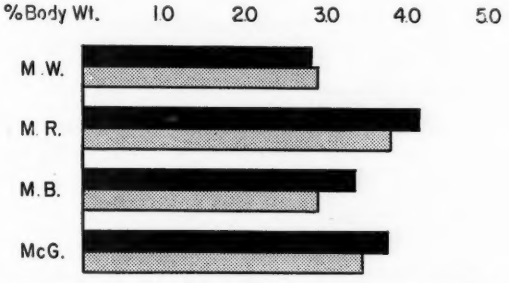

Fig. 7.—Changes in plasma volume as a result of Carbo-Resin therapy. The solid blocks represent control values, the stippled blocks the values obtained at maximal sodium retention.

The concentration of serum sodium and serum potassium remained within normal limits in all patients except E. D., in spite of the drastic reduction of available sodium. A significant drop in the carbon dioxide combining power occurred at the height of the therapeutic effect of the resin. This depression of carbon dioxide combining power in the presence of normal values for serum chloride and unchanged pH of the blood is indicative of a state of compensated metabolic acidosis.

Only minor variations occurred in the values of blood volume as a result of therapy. A breakdown of the various blood compartments, however, shows a consistent decrease in plasma volume and inconsistent changes in the red cell mass (Fig. 7). The persistent decrease in the value of blood plasma can easily be explained as an expected, compensatory reaction to maintain the status quo. This is substantiated by the constant, or relatively constant, values for serum sodium and potassium as well as by a slight increase in the values of plasma proteins. The concentration of plasma electrolytes and proteins depends on the absolute amount of the solvent (plasma). The carbon dioxide combining power, on the other hand, has no such dependence, since it is regulated by a respiratory mechanism.

The determinations of total body water on several different occasions afforded an opportunity to determine the "turnover" of water per day. The calculation of such turnover constants is best illustrated by an example:

M. R. was given 42.0 c.c. of deuterium oxide on the first day of the experimental period. Three hours following the intravenous administration of the test dose, a plasma sample was withdrawn and the deuterium oxide concentration determined. This was found to be 0.142 per cent which corresponds to a deuterium oxide space of 32,535 c.c. Seven days later another blood sample was withdrawn in order to determine the residual concentration of deuterium oxide before the infusion of an additional quantity of this tracer. A decrease to 0.060 per cent deuterium oxide per cubic centimeter of plasma was noted. Substituting these values in the familiar exponential equation,[12, 13] a fractional turnover constant of 0.123 per day is obtained. This corresponds to a turnover of 12.3 per cent of total body water per day. The deuterium oxide concentration obtained during the third determination of total body water could be utilized in similar manner. Thus, for the second period of the experiment a value of 0.107 per day was obtained which corresponds to 10.7 per cent of total body water per day.

TABLE I. CHANGES IN TOTAL BODY SODIUM BEFORE AND AFTER RESIN THERAPY

PERIOD	TOTAL BODY SODIUM IN MEQ.	TOTAL BODY SODIUM IN MEQ./KG.	PERCENTAGE LOSS OF TOTAL
Patient McG.—			
Control	2,417	42.25	
At end of therapy	1,922	33.72	20.5
Patient M. W.—			
Control	2,630	47.11	
At end of therapy	1,647	30.22	37.4
Patient M. R.—			
Control	3,678	51.29	
At end of therapy	2,470	35.44	32.8
Patient M. B.—			
Control	3,152	46.35	
At end of therapy	2,694	40.51	14.5

The results of these calculations, particularly those obtained for the first period of the experiment, represent average values only. In order to obtain the correct value for the percentage turnover per day there should be no loss of weight or body water. During the first period of the experiment there was a moderate loss of water and weight, presumably as a result of resin therapy, while during the second period the weight and total body water remained constant. The turnover per day should, therefore, be greater during the first period, which is in close agreement with the experimental findings.

Similar observations were made on the other patients in this group and the results are summarized in Table II.

The effect of the resin in diminishing the extent of proteinuria is inconclusive in our series. Only in one patient (E. D.) could a marked reduction in proteinuria be demonstrated, while all other patients showed only insignificant changes. Trivial changes in blood pressure were thought to be statistically insignificant.

All patients were able to tolerate the oral administration of the resin in amounts large enough to produce a therapeutic effect. With the exception of occasional nausea, no toxic reactions were observed. Prolonged therapy beyond the establishment of a negative sodium balance was not necessary and, because

of the brevity of the experimental period, no obvious deficiency in essential minerals or vitamins was anticipated.

In the absence of obvious renal disease, resin therapy was thought to be safe and effective in clinical practice without the elaborate studies performed in Patients 1 to 5. For evaluation of the hypothesis that the carbon dioxide combining power represents the only essential laboratory test, the two remaining patients (6 and 7) were given therapeutic doses of resins (72 Gm. per day) until the carbon dioxide combining power had dropped from about 20 to about 13 meq. Twenty-four hour urine specimens at this time showed that the urinary sodium output had dropped to zero, after 3 or 4 days of such therapy. The effectiveness of intermittent resin therapy could be demonstrated in one patient who had developed pre-eclampsia very early. This regime did prevent a premature termination of such pregnancies and its broader application should lead to a higher fetal survival in certain selected cases of pre-eclampsia.

TABLE II. COMPARISON OF HALF LIFE TIME, PERCENTAGE OF BODY WATER TURNOVER PER DAY, AND THE AVERAGE TIME OF WATER MOLECULE IN THE BODY

The values were calculated from the total body water determinations on the toxemic patients. "First" and "second" periods refer to the interval between the first and second, and second and third total body water determinations.

	HALF LIFE TIME IN DAYS	PERCENTAGE OF BODY WATER TURNOVER PER DAY	AVERAGE TIME OF WATER MOLECULE IN THE BODY
Patient M. R.—			
First period	16.6	4.16	24.0
Second period	21.0	4.00	25.0
Patient McG.—			
First period	9.4	7.2	13.9
Patient M. W.—			
First period	5.5	12.3	8.1
Second period	6.4	10.7	9.3
Patient M. B.—			
First period	16.6	4.2	23.8
Patient E. D.—			
First period	10.5	6.6	15.2
Second period	8.7	7.9	12.6

Summary and Conclusions

1. Sodium-removing resins, when administered in a dosage of 40 to 80 Gm. per day, can produce a negative sodium balance in pre-eclamptic patients who are maintained on a low-salt diet.

2. A reduction of the total body sodium of almost 40 per cent can be accomplished with this therapy. A compensated metabolic acidosis is produced, which finds its expression in a significant depression in the carbon dioxide combining power.

3. A progression of the manifestations of pre-eclampsia did not occur in those patients undergoing therapy. An example is presented demonstrating that premature termination of such a pregnancy can be prevented by judicious use of resins.

4. Repeated determinations of blood chemical values appear to be unnecessary for routine treatment of pre-eclamptic patients. Although a knowl-

edge of the 24 hour urinary sodium output appears to be desirable, in the absence of obvious renal disease, the effectiveness of the resins can be evaluated by frequent determinations of the carbon dioxide combining power, as the only essential laboratory test.

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THE VAGINAL SMEAR AS A GUIDE TO PROGNOSIS AND TREATMENT IN THREATENED ABORTION*

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FOR several years we have treated women with threatened abortion with diethylstilbestrol. We have attempted to record the results of these cases. Some of these people stopped the therapy themselves; some were inadvertently taken off the drug during the period of therapy. We have also seen some pregnant women who had vaginal bleeding early in pregnancy but did not see a physician. Many of these women had stopped bleeding by the time of the first prenatal visit. It appears from our observations that there were three types of patients with threatened abortion, classified according to response to estrogen therapy: (1) those who aborted very shortly after it was discontinued; (2) those who did not need the therapy; either they never had any estrogen, or, if they did, failed to abort when it was discontinued; (3) those who aborted in spite of the estrogen therapy.

It seems, regarding hormone deficiency, that the term "threatened abortion" does not represent one pathological entity. It is a descriptive term applicable to one of several different pathological states which may affect the ovum.

Hertig and Rock[1] and Streeter[2] feel that a large percentage of abortions are due to pathological ova. Mall[3] and Hughes and associates[4] feel that a large proportion of abortions are due to environmental abnormalities.

We know that a large percentage of bleeders do not require treatment[5, 6] and we know that some abortions are due to abnormal ova in which cases treatment is also useless. It would be of value if we could determine which cases make up that remainder of threatened abortions which treatment might help. That remainder would be caused by accidents of implantation, hydatidiform moles, acute diseases in the mother, and endocrine dysfunctions. Little can be done to salvage the pregnancy in accidents of implantation or moles. If those threatened abortions due to endocrine dysfunctions could be determined and adequate treatment started, it would be a start in the right direction.

It is now generally accepted that changes in endocrine stimulation show up in the vaginal smear.[7, 8] It is not so generally accepted that changes in endocrine stimulation in early pregnancy are evidenced in the vaginal smear. We decided to run our own series of smears and draw our own conclusions. We are by no means original in this thought. Papanicolaou, Traut, and Marchetti[7, 8] feel that the characteristics of the vaginal smear in the premenstruum

*Presented in part at a meeting of the Minnesota Obstetrical and Gynecological Society in Duluth, April 25, 1953.

are carried over into early pregnancy. Hall[9, 10] and Schneider[11] have described a process of decornification during the premenstruum and in early pregnancy. They feel this is due to estrogen and progesterone stimulation. Bonime[12, 13] describes cells which he finds in the vaginal smear of early pregnancy and which he calls functionalis cells. He attributes the appearance of these cells to estrogen and progesterone stimulation. Randall and co-workers[14] feel that they can predict impending threatened abortion by cytological means and changes in the staining reaction of the cells in the vaginal smear.

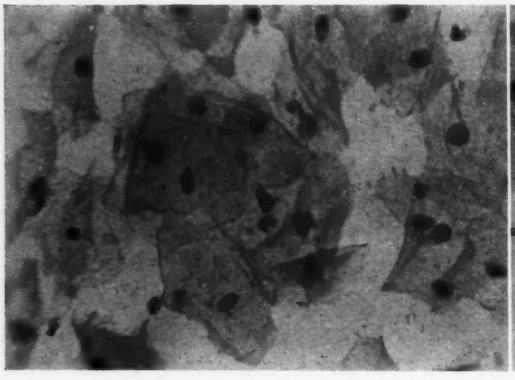

Fig. 1.

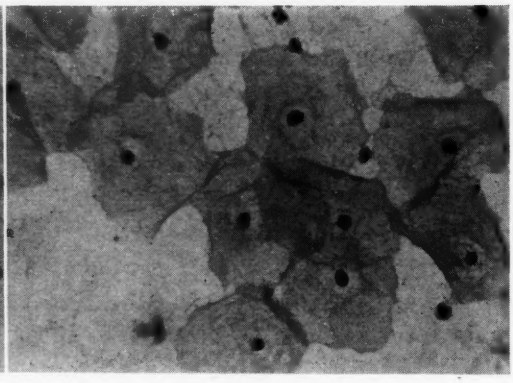

Fig. 2.

Fig. 1.—Characteristic cells found in the vaginal smear of early pregnancy. Note the large vesicular nuclei.

Fig. 2.—Mature-type cells found in the vaginal smear of most of the patients who aborted.

We collected smears from the vaginal portion of the anterior cervix in 150 consecutive cases in the first 4 months of pregnancy. This group did not contain what we considered enough bleeders for study so we collected smears, where practical, from those with a history of bleeding in the next 150 pregnancies. All of these slides were evaluated as unknowns, then compared with the patients' records. We found that most of the smears contained a great predominance of epithelial cells like those shown in Fig. 1. These correspond to the cells described by other investigators.[7-14] These cells tend to be smaller than the typical cornified cell of the vaginal epithelium. They tend to be basophilic; their edges are more distinct and are rolled; their nuclei are larger and more vesicular. Cells like this were found in great numbers in most of the smears. We feel that this type of smear may be termed a normal early-pregnancy smear. A minority of the smears contained over 30 per cent mature cells, that is, the large polygonal, clear cell, which tends to be acidophilic and has a small, very dark, pyknotic nucleus. The edges are not likely to be rolled or heavily stained. Cells like this are shown in Fig. 2. They correspond to the cells produced by estrogen stimulation in the absence of progesterone.[15] For our purposes we termed this kind of smear estrogenic.

Results

There were 20 abortions (Table I). Two of these cases were thrown out because the smears were too poor for adequate evaluation. Of the 18 remain-

ing, 12 had smears which contained 30 per cent or more mature cells. Ten had 40 per cent or more mature cells. In the cases of abortion there were 10 pathological specimens available from patients with estrogenic smears. All but one of these showed old necrotic, hemorrhagic decidua and/or sclerosed old villi. Getzowa and Sadowski[16] and Rutherford[17] have shown that these findings probably indicate that fetal death started to occur four to six weeks before the passage of the products of conception. From this one would not expect to have normal hormone stimulation. Hence an abnormal smear would be expected. Fig. 3 demonstrates one of the old villi; Fig. 4 is given as a comparison. It is a healthy villus from a normal live pregnancy of about 5

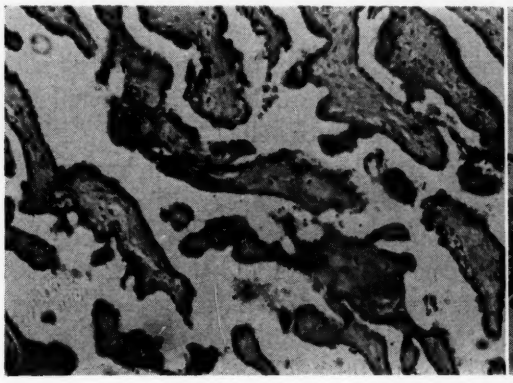

Fig. 3.

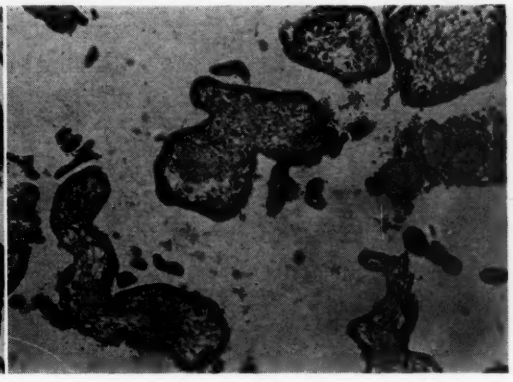

Fig. 4.

Fig. 3.—Old villi. Note the dark-staining fibrotic core.
Fig. 4.—A healthy villus from a live pregnancy of about 5 months. Compare with Fig. 3.

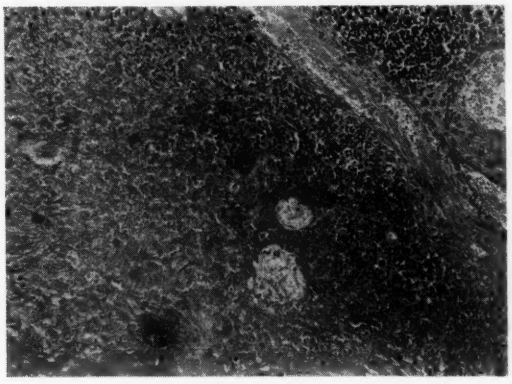

Fig. 5.—Old hemorrhagic decidua showing infiltration with polymorphonuclear leukocytes.

months. Fig. 5 shows an old hemorrhagic decidua. There were normal smears in 6 cases of abortion. Two of these had premature separations at 5 and 5½ months. Both patients delivered living fetuses. One would expect normal hormone stimulation and a normal smear in these cases. One with a normal smear had a hydatidiform mole and again one would expect at least adequate stimulation in this case. Three with normal smears who aborted showed old necrotic decidua and old sclerosed villi. We could not explain the normal smears in these cases.

TABLE I

Abortions, 18	
Abnormal smears, 12	
30 per cent or more mature cells	12
40 per cent or more mature cells	10
Old villi and hemorrhagic, necrotic decidua	9
Normal smears, 6	
Premature separation at 5 and 5½ months with live fetus	2
Hydatid mole	1
Old decidua and villi	3
Threatened Abortions, 26	
(All delivered normal term pregnancies)	
Abnormal smears, 8	
30 per cent or more mature cells	8
40 per cent or more mature cells	4
Normal smears, 18	

There were 26 patients with threatened abortions who did not later abort. Of these, there were 18 with normal smears; there were 8 with 30 per cent or more mature cells, and 4 with 40 per cent or more mature cells.

There were 44 bleeders. If we had predicted that those who had more than 30 per cent mature cells in their smears had a dead or dying pregnancy we would have been right 60 per cent of the time. If we had predicted the same for those showing more than 40 per cent mature cells we would have been right 71 per cent of the time. If we had predicted that those showing what we call a normal pregnancy smear, would deliver a normal pregnancy at term we would have been right 75 per cent of the time. If we had predicted that these same patients with normal smears had living, functioning trophoblast, we would have been correct 87 per cent of the time. These figures and their evaluation seem to reveal a useful concept in the management of threatened abortions.

Up to now we have been dealing with patients who had bleeding during the first 4 months of pregnancy. Examination of the records of the patients who did not bleed changes the picture. In the first 150 patients, 27 showed 30 per cent or more mature cells and 16 had more than 40 per cent mature cells. None of these patients had any bleeding and all had normal pregnancies.

Comment

From this small series we cannot make any definite statements. We feel that it may indicate a tendency and we have the following impressions. Assuming that the type of cells in a vaginal smear depends upon hormonal influence we might state the following: If bleeding occurs during the first 4 months of pregnancy, a smear showing large numbers of mature or estrogenic cells seems to indicate abortion at some time in the future. An estrogenic smear without bleeding during the first 4 months does not seem to carry the same poor prognosis. If bleeding occurs during the first 4 months of pregnancy, a smear which is normal for early pregnancy indicates a quite favorable prognosis. We do not know how many with abnormal estrogenic type smears could have been salvaged by therapy started when the abnormal smear was discovered. We do know that over one-half of them would have been treated unnecessarily, since in this series about one-half of the patients with abnormal smears did not bleed and had normal pregnancies.

It seems that we have not decided which cases of threatened abortion might be helped by treatment. Rather, we have shown more clearly those cases of threatened abortion which do not require treatment; that is, those showing normal smears. A significant percentage of these had living, functioning, trophoblastic tissue and delivered normal pregnancies. A goodly portion of those with normal smears who aborted had accidents of implantation. This knowledge should be of some value to one treating threatened abortions. The hormonal implications of these findings can only be guessed at.

Conclusions

1. Vaginal smears of patients with threatened abortions were compared with the smears of those who did not bleed. An attempt was made to find some difference or abnormality in the smears of bleeders which would be a guide to treatment and prognosis.

2. From these examinations a type of cell was found which seems to be normal for early pregnancy.

3. A minority of the smears showed an abnormality; there were more mature or estrogenic type cells present.

4. The patients who showed estrogenic smears and bled had a higher incidence of abortion than we usually see in a series of threatened abortions. Estrogenic smears in patients who bleed during the first 4 months of pregnancy may indicate an abnormal decidua or placenta.

5. The patients who had normal pregnancy smears and bled had a high salvage rate and at least half of those who did abort had a living, functioning trophoblast; that is, these were cases of accidents of implantation or hydatid mole. It would seem that treatment in this class of patients with normal smears is usually unnecessary or of little value.

6. It is possible that treatment might help some of the patients who show the abnormal or estrogenic type of smear.

Addendum.—Since this paper was submitted for publication, we have started treating all patients with 30 per cent or more mature cells in the vaginal smear with progesterone or placebos. The results of this study will be reported at a later date.

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CYCLIC OVARIAN FUNCTION FOLLOWING SPONTANEOUS ABORTIONS

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THERE are two distinct groups of obstetrical patients who sometimes pose similar problems. Such a problem is the return of reproductive capacity following pregnancy.

As is inferred, the first group consists of immediate puerperas. In so far as these women are concerned, this question has been studied extensively by Williams[1] in his two classic papers regarding the regeneration of the uterine mucosa and the disappearance of the placental site during the puerperium. In addition, the effects of lactation on ovulation have been fairly well documented by several authors.[2, 3] One could, therefore, give a substantial answer that pregnancy may recur as early as six weeks or as late as six months post partum depending upon whether or not lactation is maintained in the puerperium.

The other group consists of those usually distraught women who have had spontaneous abortions. The manner of disposing of this important question for this group has been completely unsatisfactory, from both the theoretical and practical viewpoints.

Rutherford and Mezer[4] attempted to follow 9 cases of spontaneous abortion by endometrial biopsies and found that ovulation occurred within the first two to three weeks after abortion. From this small number they stated that there is no endometrial evidence that this is not as good a time for impregnation as any other.

Sharman[5] studied 42 postabortal patients and found that 72 per cent ovulated prior to the first menstrual flow. Stewart[6] studied by basal temperatures a group of 27 women who "threatened" and subsequently aborted, and stated that in most cases there was an immediate establishment of a normal menstrual cycle as indicated by the biphasic character of the temperature curve preceding the onset of menstruation.

Sullivan[7] studied 75 women, also with basal temperatures, and found that 90 per cent ovulated preceding the initial "flow" and that the initial menstrual period occurred between 31 and 40 days in 75 per cent of the cases. He also concluded that, since the period of progesterone-produced hyperthermia was occasionally shorter than normal, conception prior to the onset of the initial postabortal period should not be encouraged for fear of repeat abortions.

Elsner as quoted by Sharman[5] studied 60 cases in 80 per cent of which ovulation occurred prior to the onset of the first menstrual period. Grünberger, likewise quoted by Sharman,[5] found that 67 per cent of 31 women ovulated prior to the initial period.

To gain more insight into the problem, after scanning the literature, a study was undertaken to ascertain the time of onset of cyclic ovarian function following abortion.

The group studied consisted of registered antepartum patients of the Sloane Hospital for Women. Bona fide evidence of pregnancy was obtained in each patient by curettage and histopathological examination of the tissue.

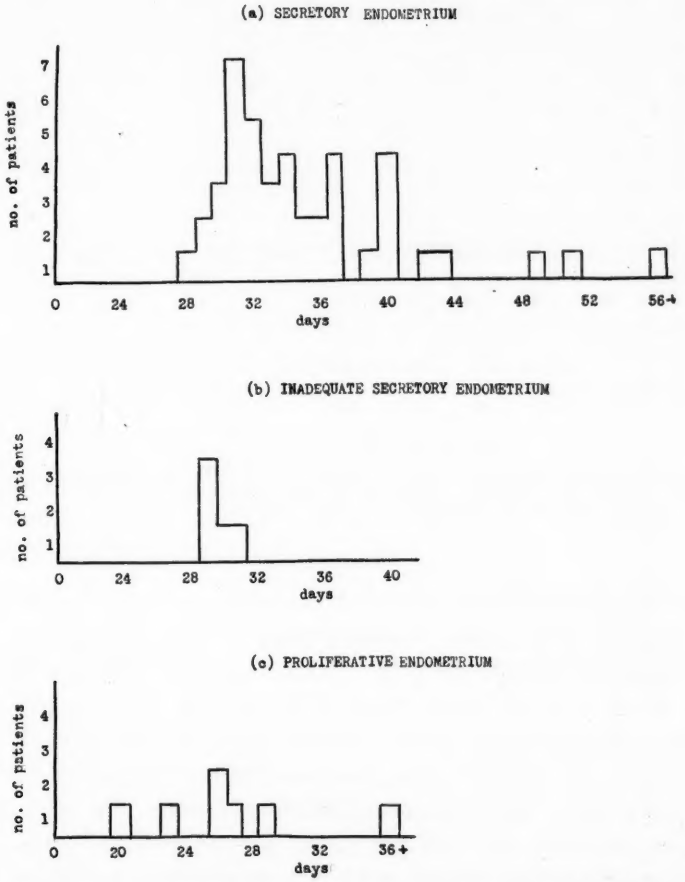

Fig. 1.—Duration of amenorrhea according to premenstrual biopsy. *a*, *b*, and *c* represent the division of the 54 patients studied according to the pathological diagnosis of the premenstrual endometrial biopsy, *a*, secretory, *b*, inadequate secretory, and *c*, proliferative endometrium, respectively.

Following a short period of hospitalization, the patients were discharged to the clinic and biopsies were taken by means of the Meigs curette at predetermined intervals dependent upon the pathological findings and their relationship to the onset of menses. Repeated biopsies were taken until normal premenstrual secretory endometrium was obtained. If the first "menstrual flow" was not preceded by normal endometrium, premenstrual biopsies were taken prior to succeeding menses.

No attempt was made to judge ovulation by daily temperature variations because of the inherent errors and the lack of correlation between ovulation time and thermal response which has been demonstrated by Buxton and Engle.[8]

A total of 54 patients were studied, of whom there were 34 multigravidas and 20 primigravidas. "Habitual aborters" and individuals with chronic systemic diseases such as diabetes mellitus and abnormal thyroid function were excluded. The period of gestation ranged from 33 days to 136 days by estimating the day of conception as being 14 days prior to the day of the first missed period.

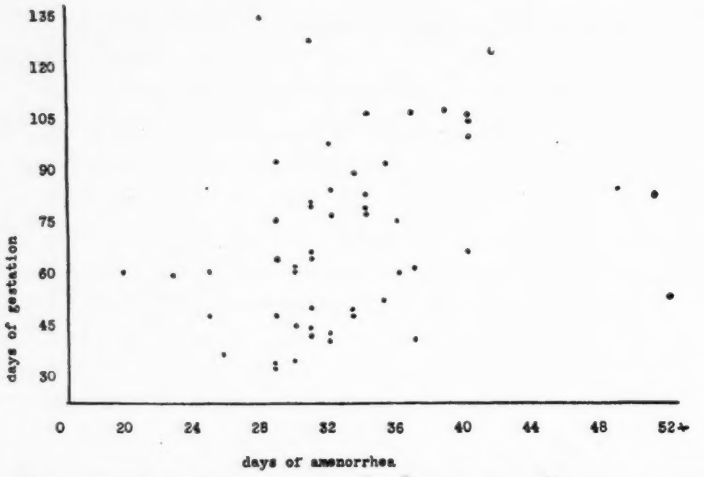

Fig. 2.—Duration of amenorrhea versus length of gestation. Each spot represents all individual patients. Note the extreme range which was found to exist, as, for example, in the group of patients whose period of amenorrhea was 29 days.

Data

A total of 84 biopsies were obtained in the previously described manner, averaging 1.6 biopsies per patient, ranging from 1 to 5 biopsies per individual.

The data obtained appear in Fig. 1, and again in a somewhat simplified form in Table I. It may be noted that 42 of the 54, or 77.8, per cent had a normal secretory endometrium prior to the onset of the initial postabortal menstrual period; 5, or 9.3 per cent, had inadequate secretory endometrium, and 7, or 12.9 per cent, had initial anovulatory cycles. In each case of the 22.2 per cent of patients who did not have normal endometrium, the second menstrual period was always preceded by a premenstrual secretory phase.

For those who had normal secretory endometrium, the average duration of amenorrhea following the curettage was 35.6 days and the mode was 30 to 31 days. Fifty per cent menstruated between 30 and 35 days. On the other hand, the average duration of amenorrhea for those who had either inadequate secretory endometrium or proliferative endometrium was 29.6 days and 25.2 days, respectively.

In Table II, the duration of gestation is compared in the three groups. No appreciable difference can be noted except that the duration of pregnancy for those who had inadequate secretory or proliferative endometrium is somewhat shortened. This may suggest the possibility of a pre-existing inadequately prepared endometrium prior to nidation.

In Fig. 2, a scattergraph is made to show the lack of correlation between the duration of amenorrhea and the duration of gestation.

TABLE I. DURATION OF AMENORRHEA

	NO.	AVERAGE	MEAN	MODE
Secretory	42 (77.8%)	35.6 days	32 days	30-31 days
Inadequate secretory	5 (9.3%)	29.6	29	28-29
Proliferative	7 (12.9%)	25.2	26	26-27

The individual cases are arranged according to the pathological diagnosis of the premenstrual endometrial biopsies prior to the initial postabortal menses.

TABLE II. DURATION OF GESTATION

	NO.	AVERAGE	MEAN	MODE
Secretory	42	73.3 days	71 days	70-84 days
Inadequate secretory	5	62.2	64	63-77
Proliferative	7	51.8	53	56-70

The individual patients are arranged according to the pathological diagnosis of the premenstrual endometrial biopsies prior to the initial postabortal menses.

Summary and Conclusions

1. Of the 54 patients studied, 42, or 77.8 per cent, had normal premenstrual secretory endometrium prior to the initial postabortal menses.

2. The average duration of amenorrhea in those with adequately prepared endometrium is slightly longer than in those with the inadequately secretory and proliferative endometrium.

3. The duration of gestation was longer in the normal secretory group.

4. The duration of gestation from 33 days to 136 days did not apparently influence the duration of amenorrhea.

5. The endometrium prior to the initial postabortal menses is not ideal for nidation.

6. A normal secretory endometrium precedes the second menstrual period after abortion.

I wish to thank Professor Earl T. Engle for his great assistance in the interpretation of many of the biopsy specimens.

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A CLINICAL ANALYSIS OF THE "ANGIOGRAMS" FOUND IN THE COURSE OF HYSTEROSALPINGOGRAPHY WITH SPECIAL REFERENCE TO TUBERCULOSIS OF THE FEMALE GENITALS

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HYSTEROSALPINGOGRAPHY is at present to be regarded as about the most important and useful diagnostic procedure for the study of sterility in women. With a popularization of this procedure, many untoward complications have occurred, one of which is represented by the unusual phenomenon of the passage of the oil-soluble contrast medium into the myometrium, vascular and lymphatic systems. The x-ray picture of this occurrence I have called an "angiogram."

Since Gajzago[2] (1931) reported one case of death due to this accident, this phenomena has been frequently called to the gynecologist's and radiologist's attention (Zacharin,[14] 1933; Shinoda[10] 1935; Lin and Tsou[6] 1935; Walter[12] 1939; Roblee and Moore[7] 1945; Keller[4] 1948; Vara[11] 1950; Karshmer and Stein[3] 1951; Drukman and Rozin[1] 1951).

An attempt was made to acquire more accurate knowledge of the causative factors in this connection with special regard to genital tuberculosis in sterile women.

Materials and Methods

Fifty-two cases of uterine "angiogram" were selected from 1,200 hysterosalpingograms taken of sterile women who visited the Department of Obstetrics and gynecology of the Tohoku University Hospital between January, 1948, and May, 1952. In addition there were 3 cases of postmenopausal women.

Hysterosalpingography was performed with the usual apparatus at an appropriate intermenstrual time, employing an iodized oil (20 or 40 per cent of Moljodol), 4 to 8 c.c. in amount, injected with pressure of less than 100 mm. hg. The pictures were taken routinely at 5 minutes and at 24 hours after injection of the radiopaque medium, and if necessary, at 15 and 30 minutes as well. In certain cases the phenomenon was directly observed under the fluoroscopic screening.

Forty-five of the 55 cases were examined for tuberculosis with the aid of repeated cultures for tubercle bacilli from the vaginal content or menstrual blood and from uterine douche fluid according to Iwabuchi-Yamaguchi's method,[8, 13] as well as endometrial or cervical biopsies. Cultures were done before or after the hysterosalpingography. In operative cases, the removed tissue was also subjected to histological and bacteriological examinations.

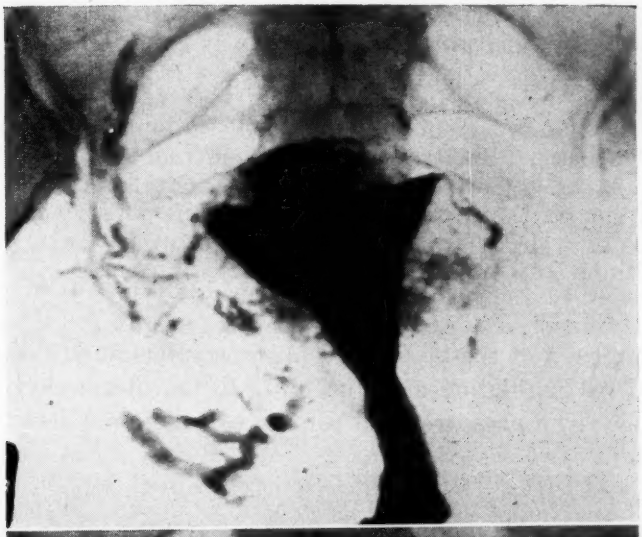

Fig. 1.

Fig. 2.

Fig. 3.

Figs. 1, 2, 3 (Case B-2291).—Patient, 27 years of age, para 0, had pleuritis 10 years before. Normal menstruation. Positive culture and positive biopsy. Ragged-wire-like and small chrysanthemum-bud-like or cherry-like shadows of the tubes are seen. (Angiogram Type A.)

Fig. 1 at 5 minutes.
Fig. 2 at 15 minutes.
Fig. 3 at 24 hours.

The hysterosalpingography was repeated in 3 patients with uterine angiograms without regard to the menstrual phase at the time of instillation. On the other hand, in order to investigate the relation to the production of the angiogram of varying pressure, amounts of radiopaque substance, and the phases of the menstrual cycle, a trial approach was made in 5 normally menstruating women after cervical dilatation and curettage with high pressure up to 250 mg. hg, and excessive iodized oil in amounts up to 20 c.c. in parts of the menstrual cycle. Trials were also made in patients with both tubes ligated but without any evidence of gynecological disease.

Results

The phenomenon of the passage from the myometrium to the uterine veins was duplicated by instillation of India ink into the uterine cavity in the operative specimens. The pressure used for the injection was less than 100 m. hg.

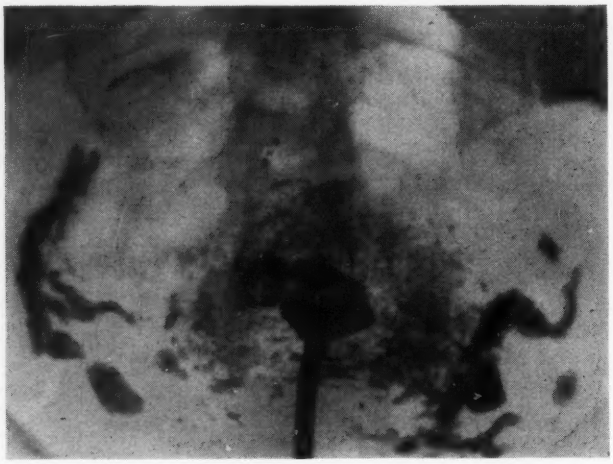

Fig. 4 (Case B-2033).—Patient, 33 years of age, para 0, had pleuroperitonitis 11 years before. Amenorrhea for 3 years. Positive culture, but the endometrial tissue could not be obtained. (Angiogram Type B.)

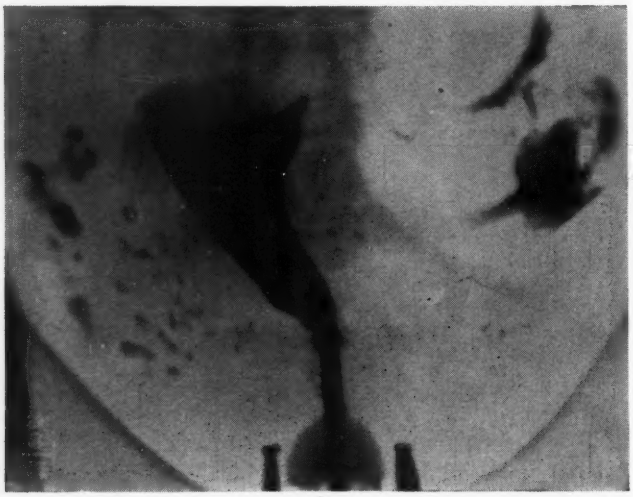

Fig. 5 (Case B-2125).—Patient, 27 years of age, para 0, had pleuritis 7 years before. Normal menstruation. Negative culture and positive biopsy. (Angiogram Type C.)

As soon as the solution was injected into the uterine cavity, the dye in the veins of the fundus began to pass quickly into the tubovarian veins, but the escape to the uterine veins seemed slower. This condition disappeared in a few minutes. With the penetration of the iodized oil into lymphatics, the x-ray picture showed a netlike uterine shadow. The residual shadow of the regional lymphatic glands usually remained in 24 hour films, and in these the radiopaque substance could be demonstrated at operation.

According to the site and mode of invasion of the radiopaque substance into the myometrium, as well as the findings of the uterus and tubes, 55 angiograms were classified into the following five varieties:

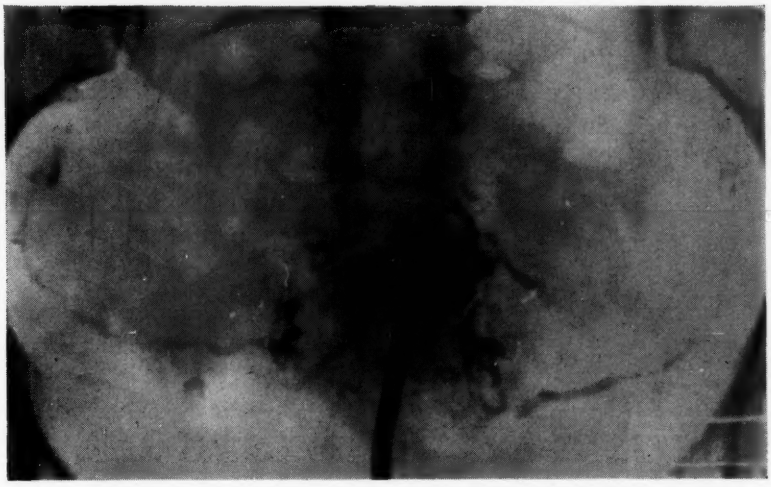

Fig. 6 (Case B-1866).—Patient, 25 years of age, virgin, had tuberculosis of lungs 4 years before. Oligomenorrhea. Typical lymphatic injection. Positive culture and negative biopsy. (Angiogram Type D.)

Fig. 7 (Case B-2192).—Patient, 30 years of age, has tuberculosis of lung at present. Hypomenorrhea. Negative culture and negative biopsy. (Angiogram Type E.)

Type A. Angiogram with normal uterine contour and blocked tubes (30 cases) (Figs. 1, 2, 3).

Type B. Angiogram with atrophic or irregular uterine contour and blocked tubes (15 cases) (Fig. 4).

Type C. Angiogram with normal uterine contour and patent tubes (6 cases) (Fig. 5).

Type D. Angiogram due to penetration of the radiopaque oil into the lymphatic vessels and glands with atrophic or irregular uterine contour and blocked tubes (2 cases) (Fig. 6).

Type E. Angiogram with uterus bicornis and blocked tubes (2 cases) (Fig. 7).

The data on all cases of angiogram are analyzed in Table I. Of 45 patients investigated thoroughly for tuberculosis, 32 cases were confirmed by means of culture or endometrial biopsies or both. In 7 cases the diagnosis was presumptive because of infertility, history of tuberculosis, menstrual disturbance, or characteristic pelvic findings. In the remaining 6 cases no signs, symptoms, or evidence of tuberculosis in culture or biopsy was to be found.

TABLE I. FIFTY-FIVE CASES OF ANGIOGRAMS

RESULTS OF EXAMINATION	TUBERCULOSIS CONFIRMED				TUBERCULOSIS SUSPECTED			TUBERCULOSIS NOT FOUND		UNEXAMINED			OTHERS	
TYPE OF ANGIOGRAM	A	B	C	D	A	B	E	A	B	A	B	C	A	C
No. of cases	18	10	2	2	4	1	2	3	3	3	1	3	2	1
Methods of Examination for Tuberculosis.—														
Positive culture	12	8	1	1	0	0	0	0	0	–	–	–	–	–
Positive biopsy	16	8	1	2	0	0	0	0	0	–	–	–	–	–
Sterility.—														
Unmarried	1	1	–	1	–	–	–	–	–	–	–	–	–	–
Primary	16	9	2	1	4	1	2	1	3	3	1	3	–	1
Secondary	1	–	–	–	–	–	–	2	–	–	–	–	2	–
Present or Previous History of Tuberculosis.—														
History of tuberculosis	12	8	1	2	4	1	2	–	–	–	–	–	–	–
None	6	2	1	–	–	–	–	3	3	3	1	3	2	1
Menstruation.—														
Normal	3	2	2	1	4	–	–	2	3	1	1	3	–	–
Disturbed	2	1	–	1	–	–	2	1	–	2	–	–	–	–
Amenorrhea	13	7	–	–	–	1	–	–	–	–	–	–	2	1
Pelvic Findings.—														
Tuberculosis	12	9	1	1	4	1	1	–	–	–	–	1	–	–
Unsuspected	6	1	1	1	–	–	1	3	3	3	1	2	2	1
Total		32				7			6		7			3
Per cent		71.2				15.5			13.3					
Total of examined cases						45								

It must be noted that there were 20 cases of amenorrhea and 4 cases of menstrual disturbance among 32 patients with angiograms and confirmed tuberculosis. Moreover, the most prominent microscopic feature of the re-

moved uterus was the inflammatory changes, especially typical tuberculous involvements, not only in the endometrium but also in the myometrium (Fig. 8). Therefore, it appears that the most probable causative factor in the production of the uterine angiogram is the extensive endometrial inflammation due to the tuberculosis.

In many cases other radiographic characteristics of female genital tuberculosis, such as chrysanthemum-bud-like or cherry-like shadow, ragged-wire-like shadow or relief shadow of the tubes were present in addition to the angiogram. These have been described in a previous paper.[5, 9]

The possible causative factor in 7 sterile women unsuspected of tuberculosis from clinical features and not checked by culture is regrettably unknown. One of them was associated with an ovarian cyst. The angiograms in 3 postmenopausal women may be ascribed to uterine damage subsequent to some unusual pathological condition, such as endometrial cancer, myomas, or an ovarian cyst.

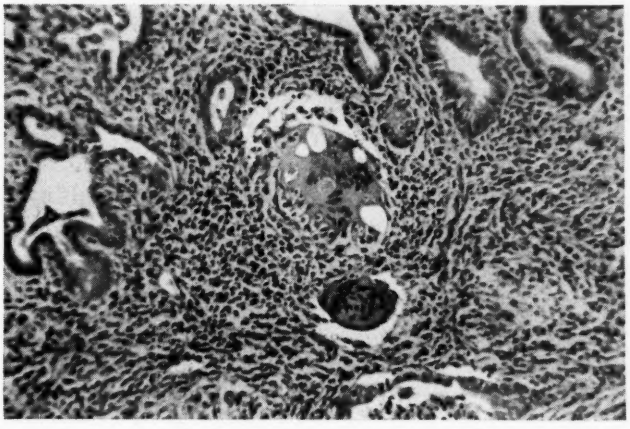

Fig. 8 (Case B-2079).—Characteristic tuberculous changes in the endometrium.

A special effort was made to investigate the influence of the menstrual cycle on the production of angiograms. Three patients with genital tuberculosis who showed the angiogram were submitted to repetitions of hysterosalpingography in the different menstrual phases. Almost identical shadows resulted. Furthermore, in the cases of apparently normal women with both tubes ligated neither a surgical procedure prior to hysterosalpingography, nor excessively high pressure, nor large amounts of the radiopaque material at the instillation caused any sign of intravascularization.

As to the patency of the tube and the form of the uterine cavity among the 55 patients who exhibited uterine angiograms, obstructed tubes (Type A) were seen in 30 (57.7 per cent); patent tubes (Type C) in 6 (5.8 per cent); and a deformed uterine cavity, i.e., atrophic or irregular uterine contour involving uterus bicornis (Types B, D, E) in 19 (36.5 per cent).

The untoward reactions associated with angiograms were the following: When the hysterosalpingography was performed about half of the patients

complained at once of smelling the iodized oil, a sensation lasting about 30 seconds. In addition, there were noted faintness, lassitude, and anorexia. A rise in temperature with chill followed the procedure in 4 cases. Neither infarct by oil embolism, nor iodism, nor irritable cough was ever observed.

Comments

As to the cause of vascularization of radiopaque material, many authors regard this phenomenon as an accident due to one of the following conditions: excess pressure employed in performing hysterosalpingography; use of too much iodized oil; unusual fragility or permeability of the vessels; open vessels in the mucosa as a result of menstruation, metrorrhagia, or old infection; decreased size of the cavity to be injected due to uterine hypoplasia or surgical removal of tubes.

Vara[11] (1950) who observed this phenomenon in 52, or 4.6 per cent, of a series of 1,119 hysterosalpingograms of sterile women concluded that the cause of what he termed a "venogram" was the underdevelopment of the uterus and occlusion of the tubes. Drukman and Rozin[1] (1951), who reported 62 cases of uterovenous and uterolymphatic intravasation, concluded that the causes cited in the literature, namely, excessive pressure, lesions of the uterine mucosa, and hysterosalpingography shortly after menstruation or curettage, did not play a major role in their series. They maintained that intravasation, under normal pressure and with patent tubes, occurred in the presence of filling defects of the uterine cavity caused by a polyp, endometriosis, or myomas. The lymphatic transfer, they believed, took place in cases with inflammatory and ulcerative processes in the uterine mucosa, inflammatory hyperplasia of the mucosa, or destructive processes in the uterine muscle. Most cases of lymphatic transfer, however, were associated with tuberculosis of the uterus and obstruction of the tubes.

Summary

1. A report is made of 52 cases (or 4.3 per cent) in which venous or lymphatic penetration of the iodized oil contrast medium occurred in hysterosalpingography of 1,200 consecutive sterile women. The x-ray pictures resulting from this phenomenon occurring after hysterosalpingography have been termed uterine "angiograms."

2. Tuberculosis was confirmed in 32 cases (71.2 per cent) by culture and biopsy methods. This diagnosis was presumable in 7 cases (15.5 per cent) and unproved in 6 cases (13.3 per cent) of 45 examined.

3. In addition to 52 angiograms in women of childbearing age, there were 3 instances in postmenopausal women associated with unusual gynecological conditions.

4. Clinical experiments revealed that an "accidental" excessive pressure, too much iodized oil, variations in the phases of the menstrual cycle, and ligated tubes seemed to have little responsibility for the production of this condition.

5. The hysterosalpingogram, if repeated in a tuberculous woman, always shows the same angiogram.

6. It must be stressed that the most prominent causative factor in the production of an angiogram in women of childbearing age is the uterine damage due to inflammatory change, especially extensive tuberculous involvement in the endometrium and myometrium which usually results in menstrual disturbances.

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CESAREAN SECTION: PROGRESSIVE TRENDS*

A Review of 852 Cases

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THE cesarean sections performed at this hospital from July, 1932, through December, 1942, have been reported in a previous paper.[11] During that time, 494 cesarean sections had been performed out of a total of 20,763 deliveries, or an incidence of 2.4 per cent. The present report covers all cesarean sections performed from Jan. 1, 1943, through Dec. 31, 1951. Of the 24,440 deliveries, 852 were by cesarean section, an incidence of 3.5 per cent.

Our purpose in writing this paper is not limited to a statistical survey of our work in this institution, but is an effort (1) to evaluate the changing indications for the performance of a cesarean section, (2) to correlate morbidity with the use of blood, antibiotics, anesthesia, type of section, length of labor, and duration of ruptured membranes, and (3) to show the resultant decrease in maternal and fetal mortality rates over the previous period in spite of (4) an increase in the incidence of cesarean section.

This series includes all cesarean sections performed in the Bronx Hospital, on either the private or ward service. All surgery was performed either by a member of the visiting obstetrical or gynecological staffs or by the resident in obstetrics, under supervision. Four hundred sixty-three cesarean sections, or 54.3 per cent, were performed on primiparas. There were 231 secondary or repeat cesarean sections, an incidence of 27.3 per cent.

In an attempt to carry through this investigation in accordance with the plan as stated above, the figures have been broken down into 3 periods of 3 years each.

Incidence

The question is often raised as to what is the acceptable incidence for cesarean sections in a teaching clinic. McCormick[1] states that the average incidence of 20 teaching clinics which he surveyed for the period of 1941 through 1945, is 3.32 per cent. Cron,[2] however, states: "We consider an incidence of 5 per cent to 5.5 per cent the irreducible minimum to which this operative treatment can be reduced."

The incidence of cesarean sections performed at this hospital for the period under analysis was 3.5 per cent. This represents an increase of 1.1 per cent over the period previously analyzed. It should be noted that during the

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3 year periods under observation, the incidence rose steadily from 2.5 to 5.1 per cent (Table I). The increase in incidence is in keeping with the feeling that the indications for cesarean section should be, and have been, extended.

TABLE I. INCIDENCE OF CESAREAN SECTIONS

HOSPITAL	TOTAL DELIVERIES	NUMBER OF SECTIONS	PER CENT
Bronx, 1932-1942	20,763	491	2.4
Millard Fillmore, 1945-1949	14,591	1,192	8.16
Pittsburgh, 1940-1949	10,499	118	1.09
Sloane, 1942-1947	17,226	1,000	5.80
New York Lying-In, 1932-1948	54,937	1,622	2.9
St. Vincent's, 1932-1946	15,429	536	3.47
Cincinnati General, 1940-1949		251	1.0
Jefferson Davis, 1941-1950	22,296	231	1.03
Norwegian, 1944-1950	10,173	400	3.93
Tennessee, 1948-1950	16,557	763	4.6
New Haven			5.9
Margaret Hague			2.6
Chicago Lying-in			5.5
Boston City			4.2
Kansas City			7.1
Johns Hopkins			5.5
Cleveland Maternity			6.1
Philadelphia Lying-In			5.8
Bronx, 1943-1951	24,440	852	3.5
a. 1943-1945	7,722	190	2.5
b. 1946-1948	9,027	271	3.0
c. 1949-1951	7,691	391	5.1
Average			4.23

Indications

The indications for cesarean sections are shown in Tables II, III, and IV. There are those individual indications which are almost mandatory for cesarean section, i.e., cephalopelvic disproportion, placenta previa, premature separation of the placenta, abnormal presentation, etc. (Table II). In addition, there are those unfavorable conditions which singly would not warrant cesarean section but, when they appear in combination with other unfavorable conditions of equal importance, offer adequate indication for section. In the latter group fall such factors as the elderly primigravida, mild toxemia, breech presentation, bad obstetrical history, and previous sterility. With the decreasing risk for the mother in cesarean section, and the greater chance of procuring a live baby from above, this broadening of indications seems justifiable. Basically, this group must be considered as an extension of indications proportionate to the value of the baby (Table III). The third group of indications encompasses those nonobstetrical conditions complicating pregnancy which are fortunately infrequently seen, but which in the mind of the attending physician justify operative interference (Table IV).

Almost mandatory indications comprised 91.5 per cent of our total. Foremost among these was previous cesarean section, 27.3 per cent. Second in frequency was cephalopelvic disproportion with or without a contracted pelvis, 22.3 per cent. Hemorrhage, including both premature separation of the placenta and placenta previa, ranked third in frequency, 14.9 per cent. Mal-

presentation was a determining factor in 8.7 per cent of our cases. This included unfavorable breech, transverse, face, and brow presentations. Fetal distress led to cesarean section in 5.9 per cent of the cases. Toxemia, including severe pre-eclampsia, eclampsia, essential hypertension, and chronic nephritis forced operative intervention in 4.2 per cent of the patients.

TABLE II. INDICATIONS

INDICATIONS	NUMBER OF CASES	PERCENTAGE
1. Previous cesarean section	231	27.30
2. Cephalopelvic disproportion	190	22.30
A. Contracted pelvis	136	15.96
B. Normal pelvis	54	6.34
3. Hemorrhage	127	14.91
A. Placenta previa	72	8.45
B. Abruptio placentae	55	6.46
4. Malpresentation	74	8.69
A. Breech	49	5.75
B. Transverse	12	1.41
C. Face	8	0.94
D. Brow	5	0.59
5. Fetal distress	50	5.87
6. Toxemia	36	4.23
7. Obstructing tumor	27	3.17
8. Previous vaginal operation	12	1.41
9. Previous myomectomy	11	1.29
10. Bad obstetrical history	6	0.70
11. Diabetes mellitus	3	0.35
12. Ruptured uterus	3	0.35
13. Cervical dystocia	3	0.35
14. Failed forceps	3	0.35
15. Uterine inertia	1	0.12
16. Old third-degree laceration	1	0.12

TABLE III. COMBINED INDICATIONS IN 59 CASES

	UNENGAGED VERTEX	BREECH	TOXEMIA	CONTRACTED PELVIS	BAD OBSTETRICAL HISTORY
Elderly primigravida	17	9	6	6	3
Unengaged vertex					2
Breech			2		2
Toxemia		2		5	3
Contracted pelvis			5		2
Sterility	1				1

Combined indications accounted for 6.9 per cent of the procedures. The elderly primigravida and the patient with a bad obstetrical history were found most frequently. Under the heading bad obstetrical history were considered those patients with previous stillbirths, previous neonatal deaths, previous mutilating obstetrical procedures, habitual abortions, etc.

A comparison of the incidence of indications in this institution with that of other institutions for a similar time period is of little value, for there is variance of opinion as to how certain obstetrical complications should be handled. For example, the range in incidence of repeat cesarean sections varies from 12.1 per cent reported by D'Esopo[3] to 32.03 per cent reported by Cody.[4] Up to the present, we have felt that almost all patients who had previous cesarean sections should be delivered by repeat section. We have always worried about the previous scar. The incidence of cephalopelvic dis-

proportion in our series was not as great as in reports from other clinics. This decrease is attributed to the liberalization of the indications for cesarean section, thereby increasing the total number of sections performed. This establishes a relative decrease of "standard" indications, rather than an absolute decrease. Further proof of this concept is shown by the increasing incidence with which fetal distress, elderly primigravida, and bad obstetrical history are factors leading to cesarean section (Table V).

TABLE IV. MISCELLANEOUS INDICATIONS

	1943-1945	1946-1948	1949-1951
1. Multiple condylomas of vulva with purulent vaginal discharge	1		
2. Fibroid uterus with chronic nephritis		1	
3. Previous operation for brain tumor		1	
4. Rheumatic heart disease, cardiac failure, and auricular fibrillation		1	
5. Uterus didelphus with pregnancy in one horn		1	
6. Syringomyelia		1	
7. Acute appendicitis at term		2	
8. Progressive laceration of cervix during labor		1	
9. Previous cerebrovascular accident		1	2
10. Progressive pyelonephritis			1
11. Rectal stricture			1
12. Rising Rh-negative antibody titer			1

TABLE V. COMPARISON OF INCIDENCE OF INDICATIONS WITH OTHER REPORTS (FIGURES GIVEN IN PERCENTAGE)

	PREVIOUS SECTION	CEPHALO-PELVIC DIS-PROPORTION	PLACENTA PREVIA	ABRUPTIO PLACENTAE	TOXEMIA
Rosensohn, Kushner, and Wahrsinger, 1932-1942	18.22	51.82	13.58	5.87	1.42
Williams and Hollenbeck, 1946-1949	30.01	28.30	12.43	4.97	6.7
Kistner, 1940-1949	22.71	51.00	6.77	5.58	3.19
Cody, 1941-1950	32.03	32.03	12.12	3.46	2.60
D'Esopo	12.1	53.9	7.6	1.8	4.1
Diddle, et al.	28.0	17.6	6.2	4.9	10.2
Zarou, 1944-1951	31.25	28.25	14.25	2.00	4.75
Posner, Cohn, and Posner, 1943-1951	27.30	22.30	8.45	6.46	4.23
Mean average	26.32	33.34	9.70	4.17	5.11

Type of Section

Table VI shows the types of cesarean sections and the incidence of each as performed during the 9 years covered by this paper. As has occurred in many other institutions, the incidence of the two-flap, low cervical procedure has increased steadily. A marked decrease in the incidence of the extraperitoneal cesarean section is a logical result of better intrapartum care, evaluation of the individual case, the use of blood, and the advent of antibiotic therapy. The grossly infected patient with prolonged labor is seldom seen now.

It is our belief that the low cervical two-flap cesarean section is the operation of choice, even in the presence of infection. However, where haste is of paramount importance, the low classical procedure should be used. We

also feel that in cases of repeat sections where multiple adhesions may make the two-flap section a prolonged, difficult, and hazardous one, the classical procedure is preferable. This is especially so where tubal ligation is anticipated. The surgeon must approach the patient with a definite planned procedure, but he must have an open mind and be prepared to change his plans.

Of interest is the constancy of the cesarean hysterectomies. From 1932 to 1942, 1.8 per cent of all sections performed here were of this type; from 1943 through 1951, the incidence was 1.6 per cent. Williams and Hollenback[5] report an incidence of 1.5 per cent.

TABLE VI. TYPE OF CESAREAN SECTION

DATES	TOTAL CASES	CLASSICAL		LOW CLASSICAL		TWO-FLAP		CESAREAN HYSTEREC-TOMY		EXTRA-PERITONEAL	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
1943-1945	190	93	48.9	12	6.3	77	40.6	3	1.6	5	2.6
1946-1948	271	88	32.5	17	6.3	156	57.6	4	1.5	6	2.1
1949-1951	391	71	18.2	25	6.4	285	72.9	7	1.8	3	0.7
Total	852	252	29.6	54	6.3	518	60.8	14	1.6	14	1.6
1932-1942	494	255	51.6			215	43.6	9	1.8	14	2.8

Anesthesia

There has been a steady trend in our institution toward the use of spinal anesthesia for cesarean sections. During the years 1943 through 1945, only 42.7 per cent of all sections were performed under this type of anesthesia. In the last 3 years, however, 76.2 per cent of the patients received spinal anesthesia. The increase in the use of spinal anesthesia has been accompanied by the marked decrease in the use of nitrous oxide-oxygen-ether anesthesia from 36.8 to 3.1 per cent. Cyclopropane anesthesia remained fairly constant with an average of 18 per cent. It is the opinion of our anesthesia department that cyclopropane is to be preferred over spinal anesthesia in the presence of hemorrhage. Many of the members of our obstetrical staff, however, prefer not to use cyclopropane. The increase in cardiac irritability and the arrhythmias produced by this drug create an increased danger in the use of oxytocic drugs. Goodman and Gillman[6] state that posterior pituitary extract has a variable effect on the heart; in some cases it causes a brief period of acceleration followed by depression; in others there is a decrease in coronary artery blood flow; while in still others there is a prolongation of auriculoventricular conduction time and sinoauricular block. The combination of cyclopropane anesthesia and oxytocic medication given simultaneously, therefore, is a decided element of increased danger to the patient.

Morbidity

Obstetrical morbidity is defined as a temperature of 100.4° F. during any two 24 hour periods following delivery with the exception of the first 24 hours post partum. In this series of cases, the morbidity rate was 49.2 per cent as can be seen in Table VII; the morbidity rate has gradually decreased from 60 to 43.3 per cent. (D'Esopo[3] reports a morbidity rate of 41.8 per cent.)

TABLE VII. TOTAL MORBIDITY

DATES	TOTAL CESAREAN SECTIONS	TOTAL CASES OF MORBIDITY	INCIDENCE (PERCENTAGE) OF MORBIDITY
1943-1945	190	114	60.0
1946-1948	271	136	50.2
1949-1951	391	169	43.3
Total	852	419	49.2

We have attempted to correlate morbidity with (1) the type of section, (2) the use of antibiotics, (3) the type of anesthesia, (4) the use of blood, and (5) the length of labor and the duration of ruptured membranes.

1. Type of Section.—There has been a gradual reduction in morbidity for all types of cesarean sections. The incidence of 47.6 per cent in classical cesarean sections, 46.3 per cent in low classical cesarean sections, and 47.7 per cent in the two-flap cesarean section shows no significant difference in these 3 types of sections. The morbidity rates of 57.1 per cent for cesarean hysterectomies and 64.3 per cent for extraperitoneal cesarean sections are understandable for, in the former, more extensive surgery has been performed and, in the latter, the indication usually was an already infected case—hence the anticipated stormy course (Table VIII).

TABLE VIII. INCIDENCE (PERCENTAGE) OF MORBIDITY IN RELATION TO TYPE OF SECTION

DATES	CLASSICAL	LOW CLASSICAL	TWO-FLAP	CESAREAN HYSTERECTOMY	EXTRA-PERITONEAL
1943-1945	59.1	50.0	59.6	66.6	100.0
1946-1948	52.3	52.9	48.1	75.0	50.0
1949-1951	40.8	40.0	44.8	42.9	33.3
Total average	47.6	46.3	47.7	57.1	64.3

2. The Use of Antibiotics.—From 1942 through 1945, penicillin was given to only 19 (10 per cent) of the patients. Of these, the penicillin was not started in 13 cases until the patient had already developed a temperature and all of these are listed as morbid. The 6 patients who received penicillin as a prophylactic postoperative measure did not develop any morbidity. During the years 1946 through 1948, the majority of the staff began to use penicillin as a routine postoperative measure; 77.9 per cent of the patients were so treated, and 52.1 per cent of these became morbid. Of the patients who did not receive prophylactic antibiotics, 43.3 per cent became morbid. From 1949 through 1951, penicillin was supplemented in several cases by other antibiotics, but these were resorted to only when the patient was already morbid, hence the exact nature and number of the cases has not been taken into account. During this period, 95.7 per cent of the patients who had cesarean sections received immediate postoperative penicillin as a prophylactic measure, but 44.1 per cent of these became morbid. Zarou[7] reports in his series of 400 cases a morbidity of 36.9 per cent where penicillin was not given and a morbidity of 13.5 per cent when prophylactic penicillin had been utilized. His total morbidity was 28.5 per cent. This difference of 23.4 per cent is impressive. Our morbidity rates are higher than those reported by Zarou. However, what does appear to be

significant is the fact that in those patients who received prophylactic penicillin, the morbidity decreased 24.3 per cent. It appears, therefore, that the use of penicillin as a routine postoperative prophylactic measure in all cesarean sections does reduce the incidence of postoperative morbidity.

3. The Use of Blood.—In the early years covered by this paper, blood was used with a certain degree of trepidation because of untoward and unexplainable ill effects on the patient. As the years passed and we came to know more about typing, Rh factor, cross-matching, Witebsky substances, etc., more blood was used. From 1943 through 1945, 20 per cent of all patients who had cesarean sections were given transfusions, and from 1949 through 1951, 43 per cent, more than twice the previous number, were so treated. The morbidity rates during this period decreased 23.1 per cent in those patients who were transfused and only 16.3 per cent in those who were not transfused. It is our belief that in addition to relieving secondary anemia, the adequate use of blood helps the body mechanisms ward off whatever is causing the morbidity, thus decreasing its incidence.

4. Type of Anesthesia.—The use of spinal anesthesia for cesarean sections has gradually increased here over the past 10 years. We have always noted a higher incidence of morbidity in those patients who have received inhalation anesthesia. However, the difference in morbidity is not clinically significant.

5. Length of Labor and Duration of Ruptured Membranes.—Other investigators have reported a steady increase in the incidence of morbidity with the increased length of time between the onset of labor or the duration of ruptured membranes and the time of operation. Carrying this line of investigation a step further, we have separated the two factors, and have compiled the incidence of morbidity for each. A morbidity rate of 43.4 per cent was found in those patients who had no labor up to 10 hours of labor and 66.2 per cent in those patients who were in labor for more than 30 hours. On the other hand, the incidence of morbidity compared to the duration of ruptured membranes, though higher than that for the duration of labor in the groups of 0-10 hours and 10-20 hours, is less than in the 20-30 hour group and shows a marked drop in those patients who had ruptured membranes for more than 30 hours (Fig. 1).

The question must be raised as to why this drop in morbidity occurred in the last-named group. It has long been a routine on our service to give all patients who have ruptured membranes for 24 hours prophylactic penicillin. We feel that this drop in morbidity is directly attributable to this use of penicillin. It is conceivable that we will be able to lower the morbidity rates even further by adopting the use of prophylactic penicillin in trial labors and prolonged labors as well.

It has long been our feeling that the use of the obstetrical standard for the determination of morbidity does not hold true in cesarean section, and we enter a plea at this time for the establishment of another standard to be used in deliveries of this type. Mason and Zintel[8] state: "It is to be expected that the temperature will be elevated 1-2° for the first 72 hours following an abdominal

operation. This postoperative rise in temperature has been attributed to absorption of blood, serum and lymph from the site of the operative incision and as an accompaniment of postoperative repair."

If we accept physiological normal temperature as 98.6° F., a 2° "normal postoperative rise" would yield a temperature of 100.6° F. which falls within the range of obstetrical morbidity. Would it not be more in keeping with clear scientific thinking to change the obstetrical morbidity standard following cesarean section to either (1) 100.4° F. temperature during any two 24 hour periods following the first 72 hours post operation, or (2) a temperature of 101° F. during any two 24 hour periods following surgery, with the exception of the first 24 hours post operation?

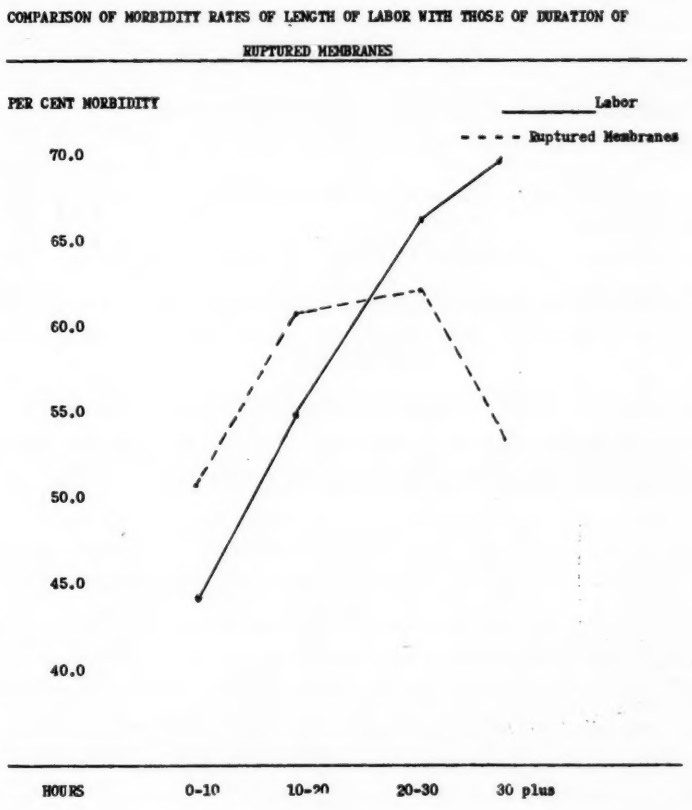

Fig. 1.

Complications

The postoperative course was marred by complicating conditions in 135 cases, an incidence of 15.8 per cent. Foremost among these was ileus which was present in 22 cases, or 2.58 per cent. Any case of distention severe enough to require treatment, e.g., gastric intubation, intravenous fluids, Prostigmine, etc., was listed in this category. Wound infection developed in 21 cases, an incidence of 2.46 per cent. In this group was considered any unusual drainage from the operative site, whether serous, serosanguineous, or purulent in

character. Thrombophlebitis was seen almost as frequently, being present in 19 cases, or 2.23 per cent. Infections of the respiratory or genitourinary systems were next in frequency, 1.53 per cent and 1.29 per cent, respectively (Table IX).

TABLE IX. COMPLICATIONS

	NUMBER OF CASES	INCIDENCE (%)
Ileus	22	2.58
Wound infection	21	2.46
Thrombophlebitis	19	2.23
Respiratory infection	13	1.53
Genitourinary infection	11	1.29
Psychosis	9	1.06
Atelectasis	6	0.70
Postpartum hemorrhage	6	0.70
Endometritis	5	0.59
Sapremia	5	0.59
Bladder injury	4	0.47
Wound hemorrhage	3	0.35
Pulmonary embolism	2	0.23
Evisceration	2	0.23
Postoperative shock	1	0.12
Peritonitis	1	0.12
Pelvic abscess	1	0.12
Cerebrovascular accident	1	0.12
Myocarditis	1	0.12
Hepatitis	1	0.12
Postoperative strabismus	1	0.12

Mortality

In the period of 1932 through 1942, the maternal mortality in cesarean sections in this hospital was 3.4 per cent and in the period covered by this report the rate had dropped to 0.59 per cent (Table X).

TABLE X. MATERNAL MORTALITY

	TOTAL CESAREAN SECTIONS	MATERNAL DEATHS	MORTALITY (%)
Bronx Hospital, 1932-1942	494	17	3.4
Bronx Hospital, 1943-1951	852	5	0.59
a. 1943-1945	190	2	1.1
b. 1946-1948	271	0	0.0
c. 1949-1951	391	3	0.8
Columbus, Ohio	523	6	1.1
Chicago Lying-in, 1931-1949	2,871		0.42
Millard Fillmore, 1945-1949	1,192	1	0.08
Pittsburgh Hospital, 1940-1949	118	0	0.0
Sloane Hospital, 1942-1947	1,000	0	0.0
New York Lying-In, 1932-1948	1,622	16	1.0
St. Vincent's Hospital, 1932-1946	536	10	1.9
Cincinnati General, 1940-1949	251		1.1
Jefferson Davis, 1941-1950	231	2	0.87
Mean average			1.19

We feel, as does Cody[4] that the prime reasons for the decrease in mortality, despite an increase in incidence of cesarean sections, are (1) increased safety of the operative procedure, (2) increased supervised training of the younger men, (3) more adequate use of blood and antibiotics, (4) better-trained anesthetists, (5) the earlier sectioning of patients before they become too exhausted

by prolonged labor, and (6) the more universal use of x-ray for pelvimetry, and to rule out fetal anomalies which might obstruct normal labor or to avoid an unnecessary section.

From 1932 through 1942, there were 28 maternal deaths in 20,272 vaginal deliveries at this hospital, an incidence of 0.14 per cent. From 1943 through 1951 there were 17 maternal deaths in 23,588 vaginal deliveries, an incidence of 0.07 per cent. Comparing these figures with the maternal death rate resulting from cesarean sections would indicate that, whereas previously submitting a woman to an operative abdominal delivery exposed her to a risk 24 times as great as from a vaginal delivery, at the present time, this risk has been reduced to 6.8 times that of vaginal delivery.

The following is a summary of the 5 maternal deaths which occurred over the 9 years covered by this report.

CASE 1.—L. B., private patient, No. 153889. Postoperative hemorrhage with irreversible shock.

CASE 2.—F. Z., private patient, No. 158833. Bilateral lower lobar pneumonia.

CASE 3.—G. K., private patient, No. 211161. Readmitted on twenty-second postpartum day with thrombocytopenic purpura.

CASE 4.—M. B., service patient, No. 229371. Cardiac arrest secondary to cyclopropane anesthesia.

CASE 5.—L. K., private patient, No. 237816. Postoperative paralytic ileus.

Obviously Case 3, idiopathic thrombocytopenic purpura, cannot be attributed to obstetrical causes and our corrected operative mortality rate would therefore be 0.47 per cent.

Fetal Mortality

There were 59 fetal deaths in this series, a gross fetal mortality rate of 6.92 per cent. In 26 of these cases, the fetal heartbeat was not heard prior to the operative procedure; in 6 cases, the fetal heartbeat was heard, yet stillborn infants were delivered. Neonatal deaths occurred in 27 instances.

Where the fetal heartbeat was not heard, the indications for cesarean section were premature separation of the placenta (19 cases), placenta previa (4 cases), contracted pelvis with cephalopelvic disproportion (2 cases), and ruptured uterus (1 case). The cases of uncontrollable bleeding speak for themselves. The 2 patients with contracted pelvis and cephalopelvic disproportion were given more than adequate trials of labor. After prolonged labor with the absence of progress, cesarean section was elected. In both instances, large babies, 8 pounds and 10 pounds, 4 ounces, respectively, were delivered. The last operation was done when a ruptured uterus was diagnosed during an attempt at vaginal delivery. At laparotomy, an anencephalic monster was delivered.

Where the fetal heartbeat was heard, cesarean section was resorted to for premature separation of the placenta (3 cases), placenta previa (1 case), ruptured uterus (1 case), and fetal distress (1 case). In the cases of accidental hemorrhage the operations were done, obviously, to control bleeding and to save the babies. Spontaneous rupture of the uterus during the thirty-first week of gestation necessitated cesarean hysterectomy. The other intrauterine death occurred in a primigravida, overdue, admitted with ruptured mem-

branes, early labor, and with a very rapid, irregular fetal heartbeat. Immediate cesarean section for fetal distress was done, but a stillborn infant was delivered. Of the 27 neonatal deaths, 18 occurred in cases of operation for placenta previa, abruptio placentae, and toxemia. All infants were either immature or premature and this accounted for the demise of the infants. In 5 other instances, prematurity was also a factor. The indications in these cases for surgery were: (1) bad obstetrical history with ruptured membranes, (2) previous vaginal plastic operation, (3) patient in labor with obstructing tumor, (4) previous cesarean section, patient in labor, (5) transverse presentation with ruptured membranes, patient in labor. Certainly, the first 2 sections were done prematurely. In the fourth case a hydrocephalic infant was delivered. In the fifth case, the infant weighed 4 pounds, 8 ounces, lived 18 days, and then succumbed to an intercurrent infection.

There were 4 full-term neonatal deaths. Two of these sections were done for contracted pelvis with cephalopelvic disproportion; 1 child died of congenital heart disease and the other of pneumonia on the sixth day of life. There was 1 case of cesarean section subsequent to failed forceps and this primary procedure probably contributed to the exitus of the infant. The last case occurred in a diabetic mother. The child had multiple congenital anomalies.

It is difficult to evaluate statistics of fetal mortality following cesarean section. Operative deliveries are done for certain definite indications and these pre-existing conditions undoubtedly affect the condition of the baby. Certainly, this mode of delivery cannot be considered at fault and the fetal mortality rate can be evaluated only with complete recognition of this fact. It would appear that the evaluation of fetal results should be considered in the light of fetal salvage, rather than of mortality rate. Our prime purpose, in most instances, is to ensure the birth of a live, viable baby. In determining fetal salvage, we cannot consider those cases in which the fetal heartbeat was not heard prior to delivery, nor those cases in which infants with congenital malformations incompatible with life are delivered. On the other hand, delivery of an immature or premature infant must be included, for a pre-existing complication of pregnancy warranted delivery at that time regardless of the condition of the infant. Neonatal death must also be included, for this hazard is present regardless of the mode of delivery. Such considerations offer a fetal salvage of 793 infants in 824 deliveries, or 96.23 per cent. It is admitted that the fetal salvage of abdominal delivery is much less than that following vaginal delivery, as was shown by Diddle and his co-workers.[9] One must bear in mind, however, that vaginal deliveries are not usually attended by obstetrical complications that are present in cases submitted to cesarean section.

The gross fetal mortality rate of 6.92 per cent shows slight improvement over the previous report of 7.26 per cent and compares favorably with statistics from other institutions: D'Esopo,[3] 3.7 per cent; Zarou,[7] 5.0 per cent; Kistner,[10] 5.1 per cent; Cody,[4] 10.8 per cent; Diddle and associates,[9] 11.38 per cent; Williams and Hollenbeck,[5] 11.66 per cent.

Summary

1. A survey of 852 cesarean sections performed during the 9 year period from Jan. 1, 1943, through Dec. 31, 1951, is presented.

2. An increase in incidence from 2.5 per cent to 5.1 per cent during the time surveyed is noted, with an average incidence of 3.5 per cent.

3. The most frequently noted indications were previous cesarean section, cephalopelvic disproportion, and hemorrhage. There has been a liberalization of indications for fetal causes, for elderly primigravidas, and for bad obstetrical history.

4. There has been a steady, marked increase in the low cervical two-flap cesarean section with a constant decrease in the classical type.

5. There has been a steady rise in the use of regional rather than inhalation anesthesia, from 42.7 per cent of cases during the first 3 years of the survey, to 76.2 per cent of the cases during the last 3 years.

6. The morbidity rate was 49.2 per cent. The use of antibiotics as a prophylactic measure in all cesarean sections has lowered the rate constantly. It is believed that penicillin should be given prophylactically to all patients in labor or with ruptured membranes for 12 hours. A plea is entered to change the obstetrical standard for the determination of morbidity following cesarean sections.

7. The chief postoperative complications encountered were ileus, wound infection, and thrombophlebitis.

8. The corrected maternal mortality rate was 0.47 per cent. One death was due to anesthesia, 1 death was due to postoperative pneumonia, 1 death was due to hemorrhage, and 1 death was due to paralytic ileus.

9. A gross fetal mortality rate of 6.92 per cent is reported. The corrected fetal mortality rate, eliminating those cases in which the fetal heartbeat was nor heard prior to surgery and cases of fetal abnormalities not compatible with life, was 3.05 per cent.

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SIMPLIFIED ROENTGEN CEPHALOMETRY

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A REVIEW of 500 cases of x-ray pelvimetry revealed that the predictability of the greatest fetal head size, occipitofrontal as well as the biparietal diameters, could be accurately determined.

The many methods of pelvimetry and cephalometry by their number would indicate that each leaves some aspect of complete accuracy to be desired. Our method is not advocated to replace any other method, but rather to add to those already in use, and, perhaps, offer a simplified method of accurately determining fetal head size.

Roentgenographic Technique

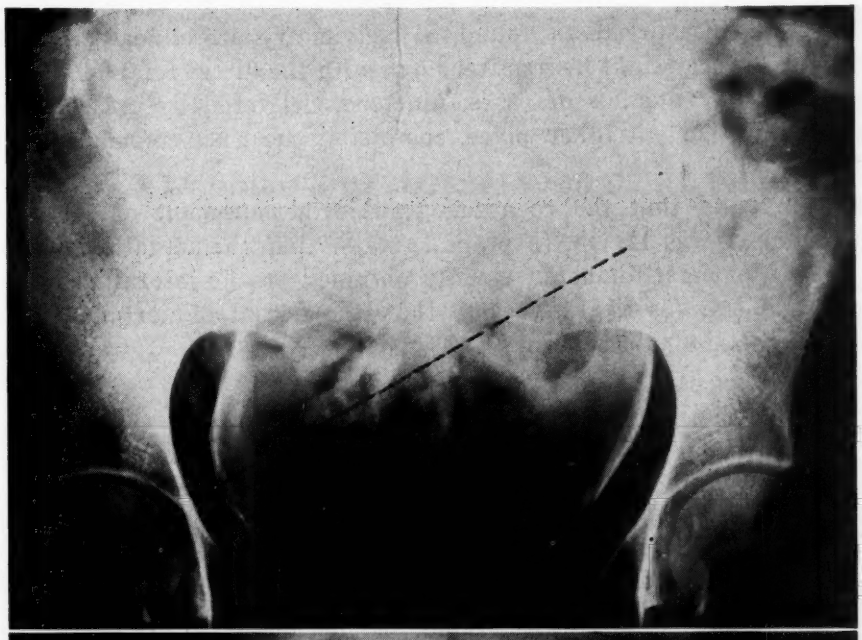
During the past two years the X-ray Department of this hospital has employed the system of Ivan Isaacs,[1] roentgen pelvimetry by differential divergent distortion. This system employs the use of three (14 by 17 inch) x-ray films taken of the pregnant patient, two of which are in the reclining anteroposterior position. These are taken at a 25 inch and 40 inch tube-film distance from the patient, and with the Potter-Bucky technique. An accurately calculated normogram is then used to determine the various pelvic diameters after they are measured from the above films. The third film is taken in a lateral projection with the pregnant patient reclining at a 36 inch tube-film distance, and with a centimeter calibrated lead rule placed between the patient's buttocks. In this hospital the earliest x-ray pelvimetry done is within two weeks of the estimated date of confinement, except under unusual circumstances. The use of this system in accurately evaluating maternal pelves in our 500 cases has proved its merit, and the reader is urged to review the original article.

Method

In Fig. 1 the occipitofrontal diameter of the fetus is measured directly from the "40 inch" anterior-posterior film. However, this is not always possible since an occiput anterior or posterior position of the fetal head will necessitate that this diameter be obtained from the lateral film. It will be shown that the difference in fetal head size on the "40 inch" anteroposterior film and the "36 inch" lateral film is negligible, and that the diameters required can be readily measured.

In Fig. 2 the biparietal diameter of the fetal head is measured directly, and, as has been stated, if the position of the head is occiput anterior or posterior, this diameter is then obtained from the anteroposterior projection.

Fig. 1.



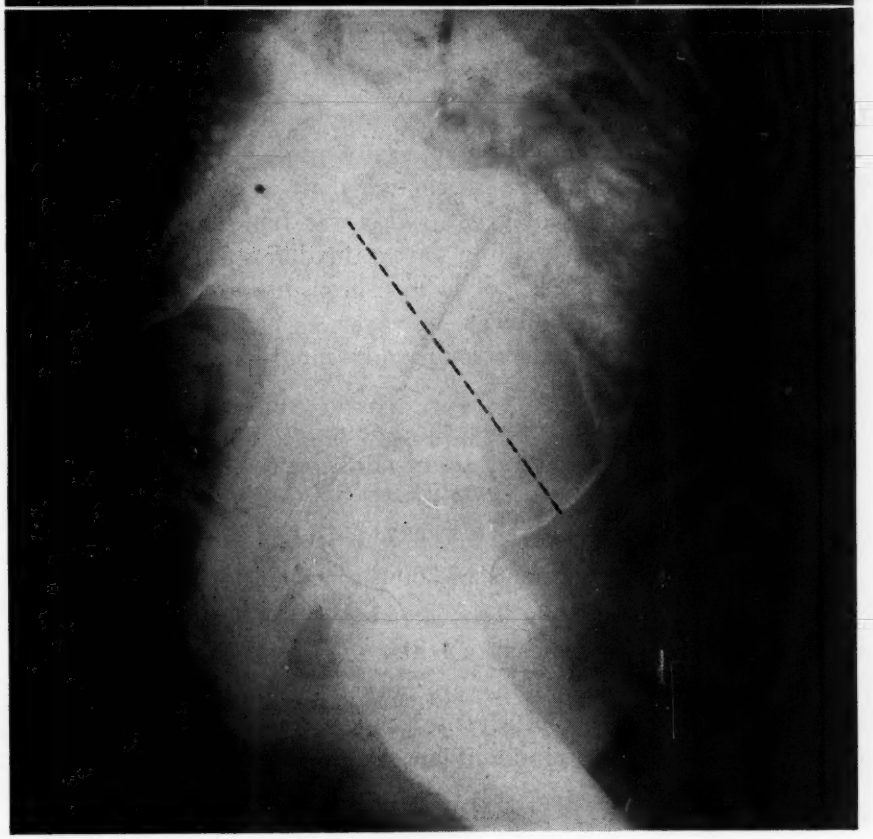


Fig. 2.

Fig. 1.—Method of obtaining the occipitofrontal diameter on the anteroposterior projection. Tube-film distance is 40 inches.

Fig. 2.—Method of obtaining the biparietal measurement on the lateral projection. Tube-film distance is 36 inches.

Case Findings

The fetal measurements found at pelvimetry were correlated within twenty-four to forty-eight hours after birth with the direct fetal head measurements. In a fair number of cases, nineteen, delivered by cesarean section where molding had not taken place, completely accurate correlation was obtained.

It was found that the roentgenographic measurement of the occipitofrontal diameter was 1.5 cm. (average) greater than the actual head measurement. The biparietal diameter, usually obtained on the lateral x-ray projection, was 1.8 cm. (average) greater than the actual clinical measurement. These data are tabulated in Table I.

TABLE I. DATA OBTAINED IN 500 CASES

	ROENTGENOGRAPHIC MEASUREMENT		DIRECT CLINICAL MEASUREMENT	
DIAMETERS	BIPARIETAL	OCCIPITOFRONTAL	BIPARIETAL	OCCIPITOFRONTAL
Extremes of measurements in centimeters	8-12	11-15.2	7-11.1	11-13

Correlation of the above revealed that:
Clinical biparietal diameters = x-ray measurement minus 1.8 cm.
Clinical occipitofrontal diameters = x-ray measurement minus 1.5 cm.

Conclusions

A review of our experiences with the previously described system would advocate this method as a simple, quick, easily applicable method of determining accurate fetal head diameters. Although there is a variable in this system which allows for error, it is not great. This was found to be plus 6 mm. and would certainly not be the deciding factor in determining vaginal delivery or cesarean section. Borderline pelvic measurements are always uncertain in prediction of the method of delivery, however, as has been aptly pointed out by Savage,[2] and a trial of labor is strongly advocated with a vertex presentation in all but grossly contracted pelves.

We do not advocate that our method be used to replace any given satisfactory method, but rather offer it as an addition to the factual already material available.

Summary

1. Cephalometric measurements of 500 cases are reviewed.

2. The factors of distortion are considered radiographically and correlated with the actual clinical measurements.

3. The actual fetal head diameters may be accurately obtained by subtracting 1.5 cm. from the occipitofrontal measurements and 1.8 cm. from the biparietal measurements as found radiographically.

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ON THE INCIDENCE OF CALCIFIED UTERINE FIBROIDS

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DURING the course of reviewing some 4,000 roentgenological studies of female genitourinary tracts made over a 6 year period, only 5 instances of calcified fibromyomas of the uterus were encountered. In an effort to ascertain from the literature the incidence of this uterine pathology, only sporadic case reports were found.

Wharton[1] averred that "complete calcification of fibromyomata uteri is not so common, but incomplete calcification is very common." Essen-Moller[2] in 1928 reflected upon his experiences in surgical excision of 1,000 myomatous uteri, but made no mention of the problem of fibroid calcification. Hunter, Smith, and Reiner[3] reviewed in 1947 their studies of endometriosis in 1,856 hysterectomies, but made no incidental reference to calcified myomas.

Tomlinson and Laird[4] recorded 4 cases of calcified uterine fibroids removed during an 8 month period in 1940. Peple[5] cited 1 case of this phenomenon in reminiscing upon some strange abdominal tumors he had chanced to find. Survey of published titles pertaining to calcified myomas of the uterus during the period 1942-1952 disclosed only 14 papers on the subject.

Possibly most of the degenerating uterine fibroids in which calcium salts are deposited cause the patient no discomfort. However, 2 of the patients described by Tomlinson and Laird[4] presented signs and symptoms suggestive of "acute surgical abdomen." Weiner, Burke, and Sherman[6] cited a case in which recurrent vesical calculi were due to bladder perforation by a calcified uterine fibroid. Rubin[7] presented 2 case reports in which symptoms of cystitis, attributed to calcified uterine fibroids, were relieved by hysterectomy.

Case Reports

Brief clinical abstracts and photographs of the radiological findings of our 5 cases of calcified uterine fibroids are submitted in this paper.

CASE 1.—Mrs. D. S., a 32-year-old white married housewife, was delivered of her third child 3 months before referral, April 4, 1953, for evaluation of urinary frequency of 2 months' duration. During each pregnancy, mild low back pain occurred in the last trimester, but not until the most recent postpartum period did dysuria and urinary frequency ensue. Concurrently, dull lower abdominal pain began. The presence of uterine fibroids had been known for 3 years, although no x-ray visualization had been done. These did not interfere with the latter 2 pregnancies or deliveries.

Menstrual history had been normal. In March, 1953, a benign cervical polyp was excised. Past history was otherwise negative.

Urinalysis revealed 4 to 8 white blood cells per high-power field. Intravenous urography demonstrated normal renal form and function. The flat abdominal roentgenogram

disclosed the calcified fibroids seen in Fig. 1. By cystoscopy, trigonitis and urethritis with numerous stringy polyps were observed; there was external pressure indentation against the base of the bladder and the right lateral wall, presumably due to the uterine fibroids. Gantrisin relieved the urinary symptoms within 7 days.

Hysterectomy was performed by the referring gynecologist April 20, 1953. No urinary symptoms recurred postoperatively.

Comment.—No genitourinary manifestations resulted from fibroids of 3 years' duration until a second pregnancy was completed. Dull abdominal pain and cystitis developed in the latter postpartum period. Hysterectomy relieved the symptoms.

Fig. 1 (Case 1).—Two discrete, lightly calcified uterine fibroids in young, white multipara. Dysuria relieved by hysterectomy.

CASE 2.—Mrs. L. R., an 80-year-old white widow who had had 2 children 50 years before, underwent surgical repair of a cystocele in October, 1952, elsewhere. Postoperatively and until seen in this office March 16, 1953, she suffered urinary incontinence unrelated to stress, and also dysuria with urinary frequency.

The past history was essentially negative. Her health had always been good. Menstruation had terminated easily 35 years previously.

An obese, healthy old woman, she had slight suprapubic tenderness on deep palpation. On pelvic examination, a small, recurrent cystocele was seen; otherwise manual palpation was negative. However, exquisite tenderness was noted in response to pressure against the base of the bladder. Innumerable pus cells were seen microscopically in the centrifuged urinary sediment; numerous bacilli and cocci were present in the stained smear. Cystoscopy revealed an irritable bladder of reduced capacity, superficial mucopurulent exudate at the left posterolateral wall and 2 intensely inflamed areas in the dome of the bladder strongly suggestive of interstitial cystitis. Clear urine spurted from each ureteral orifice. Bilateral retrograde pyelograms produced the film shown in Fig. 2.

Bacteriological culture of the bladder urine grew *Proteus rettgeri* resistant in vitro to all antibiotics except Chloromycetin. Several days' use of this drug effected marked relief of symptoms.

Comment.—Whether the relatively small degree of calcareous degeneration within a uterine fibroid—or the fibroid itself—precipitated the cystitis is doubtful. The bladder inflammation responded promptly to proper antibiotic therapy.

CASE 3.—Miss C. L., a 69-year-old white spinster, was referred Feb. 23, 1953, for evaluation of moderate urinary frequency of 25 years' duration. Intermittent, dull, left lower quadrant abdominal pain for the past 10 years was actually the primary complaint. Two years previously, study of the pain elicited the advice that a uterine fibroid was present; she was warned against surgery.

Menstrual history had been normal. Menopause took place uneventfully 20 years before.

Only slight tenderness in the left lower abdominal quadrant was found by examination. The senile virginal vaginal introitus was too tight for digital investigation. Urine was microscopically negative. Plain abdominal roentgenogram disclosed the calcified uterine fibroid shown in Fig. 3. No therapy was given.

Fig. 2 (Case 2).—Spotty calcification within fibromyomas of the uterus discovered by study of bladder infection in 80-year-old white multipara. Antibiotic therapy only.

Fig. 3 (Case 3).—Huge, solitary, heavily calcified uterine fibroid in aged, white spinster; caused minimal symptoms. No treatment.

Four days later the patient stated that she was asymptomatic. She requested deferring cystoscopy and bilateral retrograde pyelography.

Comment.—Massive calcification within a nulliparous uterus, presumably of 25 years' duration, produced negligible symptoms. No therapy was required. Hysterectomy was not advised.

CASE 4.—Mrs. R. R., a 53-year-old Negro woman who had had one child 30 years before, was referred July 15, 1948, for sudden, painless, profuse hematuria of 5 days' duration. Aside from slight suprapubic discomfort and moderate increase in urinary frequency since onset of the urinary bleeding, there had been no previous nor associated genitourinary disorders. Her general health had always been and remained good.

The past history was negative. The menopause had occurred 17 years before; there were no sequelae.

Fig. 4 (Case 4).—Arborizing, extensively calcified uterine fibroids in hypertensive, 53-year-old primiparous Negro woman; caused painless, profuse hematuria. Cured by hysterectomy.

No gross abnormality was discerned in this slender, healthy-looking woman, although the blood pressure was 200/110. A smooth mass in the midline of the lower abdomen extended to the umbilicus and to an indeterminate distance below the symphysis. Pelvic finding of a tremendously enlarged, hard, nodular, fixed uterus identified the origin of the abdominal mass. Microscopic urinalysis revealed 40 to 50 erythrocytes and rare leukocytes per high-power field.

Cystoscopic evaluation was limited by bladder distortion due to extrinsic uterine pathology. No intravesical abnormality was seen. Ureteral catheterization recovered grossly bloody urine from each side. The retrograde pyelogram is shown in Fig. 4.

Hysterectomy was performed elsewhere 2 weeks later. Hematuria never recurred, according to letters from her referring physician attesting also to her continued good health, free of hypertension.

Comment.—The extensive calcific degeneration within fibromyomas of the uterus exerted great pressure upon the bladder. It may be supposed, in retrospect, that this caused hematuria as a mechanical vascular congestion within the ureters. The bladder itself was not bleeding when observed cystoscopically; the pyelograms demonstrated relatively normal renal morphology. It is of interest that hysterectomy coincidentally relieved the hypertension.

CASE 5.—Mrs. G. G., a 75-year-old white married, nulliparous woman, was referred Sept. 30, 1947, for urological study of severe right lower quadrant abdominal pain of 1 week's duration. The pain had subsided gradually within an hour, but residual discomfort persisted, identical with that experienced at that site for the past 5 years. Nocturia had developed, about 2 to 3 times nightly, during the past decade.

The past history was irrelevant. The menopause had supervened uneventfully 30 years before.

There was moderate tenderness in the right lower abdominal quadrant. No abdominal mass was felt, but by pelvic palpation a nodular, firm, movable, slightly tender mass was detected within the uterus. Microscopic urinalysis disclosed rare erythrocytes and leukocytes. Intravenous pyelography demonstrated the uterine calcification illustrated in Fig. 5. Aside from slight blunting of the left renal calyceal system, renal morphology and physiology were normal.

Fig. 5 (Case 5).—Irregular, totally calcified uterine fibroid occupying most of true pelvis but producing negligible abdominal or urinary symptoms in 75-year-old white multipara. Symptomatic treatment.

The patient was returned to her physician who successfully prescribed palliative therapy for the bladder symptoms. The patient was killed in an automobile accident 6 months later.

Comment.—Only dull lower abdominal pain of 5 years' duration attended this patient's calcified uterine fibroids. Cause of the acute abdominal pain which led to medical study was not clear. Symptomatic treatment of persistent, dull abdominal pain and of urinary frequency sufficed to control this elderly woman's discomfort.

Comment

Calcified uterine fibroids were discovered by urological x-ray examination of the abdomen in 5 patients, aged 32, 53, 69, 75, and 80 years. Four were white and the other a Negro. Bladder symptoms were prominent in 4 women, in one of whom massive hematuria occurred. The fifth patient suffered chronic lower abdominal pain which became inexplicably acute, only to subside spontaneously. In the two youngest patients hysterectomy fully relieved the complaints. No treatment was necessary in another patient; the remaining two were adequately relieved by anodynes and/or antibiotic therapy. In none was the preradiological diagnosis suspected, although obviously abnormal uterine findings on pelvic examination indicated further study in each case.

Summary

Five instances of extensive calcification of uterine fibroids were found in over 4,000 abdominal x-ray examinations in the course of urological study. All except one of the patients were over 50 years of age. In 4 women, bladder symptoms were prominent; all had varying degrees of lower abdominal discomfort.

Calcification within fibromyomas of the uterus is an apparently innocuous phenomenon, per se, but can produce dramatic pressure effects upon near-by structures.

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THE ABDOMINAL APPROACH TO CYSTOURETHROCELE REPAIR

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THE problem of inefficient or incompetent urinary bladder function is an ever-prominent concern in the field of gynecology. Since the early contributions of Kelly[1, 2] and Baldy[3] many investigators both in this country[4-16] and abroad[17-19] have described different operative repair or reconstruction techniques in attempts to deal successfully with the problem of bladder, urethra, and/or terminal rectum herniation. Recently we have also seen a marked increase in investigative interest aimed toward a basic comprehension of physiological urinary bladder function.[20-23] Despite these widespread efforts, there has been too little emphasis on the frequently recurring problem of the patient who presents simultaneously two basic gynecological complaints: (1) a pelvic distress syndrome associated with a cystourethrocele and/or rectocele, (2) concomitant pelvic pathology which individually warrants surgical intervention.

Such patients have on occasion been subjected to one of three procedures. First, separate operations were performed at different times necessitating two different anesthetics. Second, both the abdominal and vaginal operations were carried out under the same anesthetic, the vaginal repair work initiated immediately following the termination of the necessary abdominal procedures. Certainly the combined procedure has been a lengthy and exhausting one, not only for the patient, but for the operating team. Third, the technique of vaginal hysterectomy has been of major moment in solving the problems of combined pathology when the abdominal component involves an operable uterus.

The technique emphasized below is suggested for those patients whose herniation symptoms exist to an embarrassing degree, yet in whom vaginal hysterectomy is not the operative procedure of choice due to the particular abdominal pathology present. Examples of this type of situation would include those patients with excessively large uterine myomas. widespread previous pelvic infection, or endometriosis with resultant embarrassing adhesions, and various types of ovarian tumors, such as a pseudomucinous cyst or a dermoid. No claim is made for originality of basic technique. Marek,[24] Weinstein,[25] Schauffler,[26] and Macleod[27] have discussed the basic technique in recent publications. These men, however, have limited the abdominal approach to cystocele repair alone. It is perfectly possible to continue the surgery to include repair of a urethrocele at the time of the cystocele repair. Although this method of repair has certain restrictive limitations, which will be subsequently described, the technique is a useful supplement to the routine gynecological armamentarium.

Procedure

The success of the entire surgical procedure is dependent, as always, upon exposure. If abdominal hysterectomy is indicated and a cystocele and/or urethrocele also need attention, intra-abdominal exposure of the herniation sites beneath the bladder and urethra may be accomplished with relative ease. The bladder flap is raised from the anterior wall of the lower uterine segment after the round ligaments are isolated, ligated, and marked. At this juncture, however, it is most important to dissect the avascular spaces bilaterally to the uterine vessel site. Dissection of the avascular spaces to the pelvic wall will allow easier and wider separation of the bladder from the anterior vaginal wall and subsequently facilitate mobilization of the urethra.

Once the bladder flap is identified and raised, laparotomy sponges may be used for further dissection and for packing to protect the freshly exposed posterior wall of the bladder which is easily raised from the anterior vaginal wall by blunt dissection. Once the dissection reaches the level of the urinary trigone upward pressure on the bladder fundus will place tension on the ureters and allow their easy identification. Further dissection, confined to the midline, will demonstrate the herniation site beneath the urethra.

With the entire bladder packed away from the anterior vaginal wall, the proposed hysterectomy can be carried out with increased efficiency. Once the cervix has been removed, the wound in the vagina closed, and the paracervical fascia brought to the midline as a secondary cuff support, the herniation site between the widely separated leaves of the pubocervical fascia, as demonstrated by Fig. 1, may be attacked.

Stay sutures are placed at either side of the recently sutured vaginal cuff. These sutures are for retraction purposes only and are removed subsequent to the completion of the surgery. Tension on these sutures and retraction on the bladder mass (protected by the previously described packing) will free the surgical field and provide all necessary exposure.

The fascial separation is quickly and easily repaired with No. 00 chromic catgut and the use of the interrupted suture technique. The fascia is first brought to the midline about halfway between the apex of the vaginal cuff and the bladder trigone region. There is less tension here, allowing easier approximation in the midline for the separated fascial layers. This technique also makes tissue identification easier at the apex of the vaginal cuff, where operative procedures, such as removal of the cervix, frequently make satisfactory fascial layer identification difficult. Subsequent sutures close the herniation site from the trigone area to the apex of the vaginal cuff, as shown in Fig. 2.

Vein retractors are then placed beneath the bladder trigone and with elevation here and cephalad tension on the vaginal cuff stay sutures, the operative site beneath the urethra becomes available. Small round needles (Ferguson No. 12) and No. 000 chromic interrupted catgut sutures may be used to repair the herniation site from the trigone area to the base of the urethral meatus. It is important to investigate the lateral pubocervical fascia

planes at this point for lacerations that may angle away from the midline. Many vaginal-approach urethrocele repairs are subsequently found to be unsatisfactory due to the failure of the operator to take into account the fact that, beneath the urogenital diaphragm, the posterior wall of which is formed by the pubocervical fascial layer, fascial tears are frequently found in horizontal planes in addition to the usual midline separation. Any such defects may be repaired as easily from above as from below, if they are clearly demonstrated.

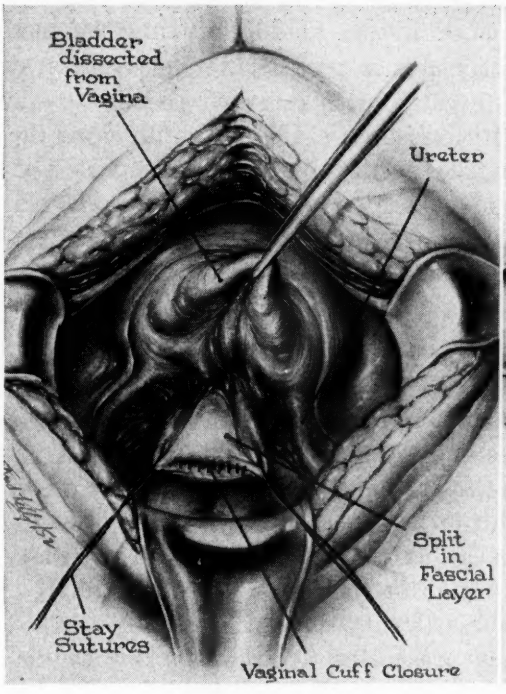

Fig. 1.

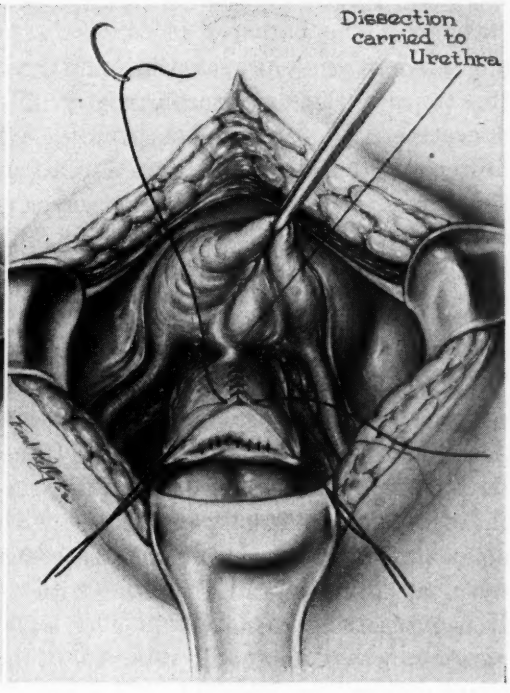

Fig. 2.

Fig. 1.—Demonstration of herniation site between leaves of pubocervical fascia.
Fig. 2.—Closure of herniation site from the trigone arc to the apex of the vaginal cuff.

Once the fascial defects have been repaired and the round ligaments and sacrouterine ligaments brought to the vaginal cuff for support, the entire area is reperitonized in the usual manner using the bladder peritoneum for the process. When the bladder packs are removed, there is little or no bleeding from the base of the bladder as the packing technique has also provided a useful hemostatic effect.

When the abdominal component of the operative procedure is satisfactorily completed, the patient is placed in lithotomy position and draped in the usual manner. Careful examination at this time will demonstrate the suture line in the pubocervical fascia extending from the vaginal cuff to the urethral meatus. The sutures may be palpated easily through the redundant vaginal mucosa which will be seen hanging from the anterior vaginal wall in the midline. This excessive mucosa is usually removed during routine pro-

cedures for cystourethrocele repair, when the operative approach is through the anterior vaginal wall from below. No attempt is made to remove this mucosa, when the approach is from above. Complete tissue retraction will have occurred by the time the patient returns for a six weeks postoperative examination. In fact about 50 per cent retraction will be demonstrable by the time the patient leaves the hospital eight to twelve days after surgery.

If a rectocele is present, a posterior colporrhaphy may be carried out at this time, using the usually accepted techniques for the procedure.

The patient leaves the operating room with an indwelling bladder catheter. The catheter is routinely placed in the bladder during the preoperative vaginal preparation, and greatly aids in identifying the urethra at the time of the urethrocele repair. The catheter is removed the first postoperative day. Spontaneous voiding with less than a 100 c.c. residual on the first check has been the rule for all of the twenty-five patients reported in this series. In a recent case, however, poor bladder tone and a 200 to 300 c.c. residual urine were encountered. This patient took five postoperative days before she developed complete control and could satisfactorily empty the bladder.

Results

Twenty-five operative cases have been followed for periods of time ranging from a maximum of three and one-half to a minimum of one year postoperatively. Twenty-three of these individuals have not only been relieved of the distresses occasioning the laparotomy, but have also lost all of the symptoms normally associated with the presence of a cystocele, urethrocele, and/or rectocele. Such distresses as urinary frequency and urgency, dysuria, polyuria, and dribbling with a cough or sneeze have been eliminated. It is interesting to note that each of these twenty-three successfully treated patients was completely relieved of her presenting symptoms prior to discharge from the hospital. The hospital stay for the twenty-five operative patients ranged from seven to twelve days.

Two patients have had operative results that could not be termed satisfactory. In both instances, the patients continued to present symptoms associated with a persistent urethrocele after the surgery was completed.

The first patient (No. 4 in the series) weighed 242 pounds at the time of surgery. She was operated upon for a large myomatous uterus that reached to the umbilicus. In addition to complaints associated with the tumor, she had the usual symptoms associated with an advanced cystourethrocele and did, in fact, have these findings at pelvic examination. She had had three children (the youngest 15 years) and dated her urinary difficulties from the birth of the second child, a 10 pound infant born by breech delivery. At laparotomy, a satisfactory result was thought to have been obtained in repairing her hernias by the abdominal approach, even though exposure of the urethra was extremely difficult due to the patient's obesity. Subsequent to abdominal closure, however, when the patient was placed in lithotomy position to check the surgery, and to complete the operative work with the minor

posterior colporrhaphy that was indicated, it was obvious that the sutures placed from above terminated at least 2 cm. from the urethral meatus. Since the patient was operated upon early in the investigative series, nothing further was done from below and the result in her case was evaluated purely in the light of an admittedly limited abdominal approach. She was relieved of her cystocele symptoms immediately, but continued to complain of the embarrassment associated with urinary dribbling on coughing and sneezing. The patient's symptoms persisted for six months postoperatively. She was then readmitted, and the residual urethrocele repaired satisfactorily under local anesthesia.

This particular case points out one of the acknowledged shortcomings of the proposed operative technique. If the patient is excessively stout, it may be impossible to expose successfully the fascial separation along the posterior leaf of the urogenital diaphragm. If such a situation exists, time may still be saved by repairing the cystocele from above and completing the urethrocele repair from below. Had this patient not been operated upon so early in our series, it is probable that she would have been so treated. As it was, she served to point out one of the operative limitations of the technique.

The second failure (operative Case 19) also retained the symptoms of dribbling urine with coughing and sneezing during the immediate postoperative period. Since this patient was further along in our operative series, her continued complaints in the immediate postoperative period brought early attention. Ten days after the primary surgery, the urethral area was explored under local anesthesia and a horizontal tear in the posterior leaf of the urogenital diaphragm, completely overlooked at the operative table, was noted. The tear ran laterally from the midline at nine o'clock and continued to the pubic ramus. The fascial rent was repaired easily and the urinary symptoms immediately controlled. This patient was discharged forty-eight hours later after a twelve-day total hospital stay.

Again the untoward result was upsetting, but, as a case in point, served to emphasize a second shortcoming of the technique. It is difficult to secure sufficient exposure beneath the urethra to repair fascial tears that angle from the midline toward the pelvic brim. Such defects may be easily overlooked unless the operator is particularly alerted to the situation. If the patient is obese, as previously described, it might be impossible to repair completely such a fascial tear from above, but five minutes' dissection and repair would complete the task, when the patient is examined in lithotomy position after completion of the abdominal procedures.

Comment

The operative technique involved in repairing a cystocele and urethrocele from above, and an evaluation of the results obtained with the technique have been presented in detail. It is important to emphasize the fact that the surgical procedure is essentially uncomplicated, and that a clinically satisfactory result is entirely dependent upon successful surgical exposure

of the operative site. The technique of repairing a cystocele from above has been described in detail by other writers as noted earlier. The urethrocele repair is the simple continuation of a similar surgical technique to include the posterior leaf of the urogenital diaphragm.

The technique is of real value in operative cases in which a hysterectomy is indicated, yet a vaginal hysterectomy is not considered the treatment of choice. The technique has been described primarily to fit this clinical picture. In addition, frequently abdominal exploration is indicated without the ultimate necessity of carrying out hysterectomy procedures as, for instance, in a case of widespread endometriosis or of a large ovarian cyst. If these patients have, in addition, the complaints and pelvic findings associated with a cystocele and/or urethrocele, these hernias may be repaired from above, and a significant amount of operative time saved or even the possibility of two separate operative procedures avoided.

It is imperative that the anterior vaginal wall be examined subsequent to the completion of the abdominal procedures, before the anesthetic agent is discontinued. If the interrupted sutures used to repair the urethrocele have not been placed to within approximately 1 cm. of the urethral meatus, terminal sutures to complete the urethrocele repair may be necessary and can be placed immediately with a minimum of effort. Additional suturing will be necessary only when patients are excessively obese or when a lateral tear from the midline cannot be successfully exposed from above.

A successful surgical procedure will alleviate all of the symptoms associated with a cystocele or urethrocele while the individual is still in the hospital. If urethrocele symptoms such as the dribbling of urine with coughing or sneezing persist beyond one week postoperatively, the repair is probably faulty. In such instances a minimal exploration under local anesthesia will demonstrate the fault. Usually the difficulty will lie in the direction of horizontal tears in the pubocervical fascia, as it forms the posterior leaf of the urogenital diaphragm. These tears angle away from the midline, usually at ten or two o'clock, and frequently extend to the pubic ramus. Failure to close these secondary lacerations successfully will usually result in ultimate failure of the urethrocele repair, whether the surgical approach be from above or below.

As a side issue, familiarity with this technique will result in the repair of many an incipient cystocele at the time of a routine abdominal hysterectomy procedure. Such a patient may have no clinical symptoms associated with a cystocele or urethrocele at the time of surgery, yet, in many instances, a complete abdominal hysterectomy has been followed by herniation of the bladder through the remains of the pubocervical fascia, initiating clinical symptoms and necessitating a subsequent repair procedure from below. Careful inspection of this fascial sling during a hysterectomy, when the bladder has been raised from the lower uterine segment and the anterior vaginal vault, may show separation of the two leaves of the pubocervical

fascia from the midline as demonstrated in Fig. 1. If the incipient hernia is noted, it is indeed a simple procedure to repair the potential defect, subsequent to the removal of the cervix.

If the patient is in the premenopausal age group with satisfactory estrogen production, pelvic relaxation may not have become a problem, and physical findings associated with a cystocele may have remained of minimal import. If the potential herniation site is not repaired, many of the patients must return for further surgery subsequent to estrogen withdrawal, or gradually become pelvic cripples for lack of the contemplated surgery. Many a five-year poor result has developed subsequent to satisfactory hysterectomy technique because the operator has not taken the five minutes necessary to repair the potential herniation site, when surgical exposure at the time of the hysterectomy made the operative field easily available. This oversight usually occurs, of course, because the operator has not been alerted to the potential danger of the situation.

Summary

A technique for repairing real or potential cystoceles and urethroceles from above at the time of otherwise necessary abdominal exploration has been described and discussed. The application of this technique and its surgical indications are commented upon. The surgical failures are described in detail and the limitations of the technique defined.

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SARCOMA OF THE UTERUS

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SARCOMA of the uterus was first described in 1860, when the first case was presented to the Berlin Obstetrical Society by Carl Meyer.[1] Rudolf Virchow[2] made the pathological report on this case. The earliest significant report in the United States was not until 1894 when J. Whitridge Williams[3] published a monograph on the subject. Although not very common, it is by far the most common sarcoma of the genital tract. Because of its relative infrequency, publications on the subject are few, and this report may add to our understanding of this malignant disease.

Incidence

The records of the Louisville General Hospital during the past 24 years list the diagnosis of sarcoma of the uterus in only 17 cases. The slides and clinical histories were reviewed and 2 cases previously diagnosed as leiomyosarcoma were excluded because of the lack of histological proof of malignancy. These were reclassified as highly cellular leiomyomas. During this period, 1927 through 1950, there were 17,759 patients admitted to the Gynecological Service; therefore the incidence of sarcoma of the uterus was less than 0.1 per cent of all admissions. As noted in Table I, there were 737 cases of carcinoma of the uterus; hence sarcoma constituted 2 per cent of uterine malignancies and the relationship of sarcoma to carcinoma was 1 to 49. Since 3,443 myomas were observed, 9, or 1:382, or 0.26 per cent showed sarcomatous changes.

TABLE I. INCIDENCE OF SARCOMA OF THE UTERUS AT LOUISVILLE GENERAL HOSPITAL (1927 THROUGH 1950)

	NO. CASES
Total admissions to gynecological service	17,759
Leiomyoma of uterus	3,443
Carcinoma of uterus (cervix and fundus)	737
Sarcoma of uterus	15
Primary	6
Secondary	9
Incidence of sarcoma	
As to gynecological admisisons	0.08%
As a malignant tumor of the uterus	2.0 %
Ratio of sarcoma to carcinoma	1:49
Associated with myomas (secondary sarcoma)	0.26%

Table II shows the ratio of sarcoma to carcinoma as reported by different authors. As one can readily see there is a great variation in these reports.

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Randall[4] reported 39 cases of sarcoma of the uterus and these constituted 6.3 per cent of all uterine malignancies, giving a ratio of 1 sarcoma to 15 carcinomas. Thornton[5] reported 24 cases of sarcoma and these constituted 1.5 per cent of all uterine malignancies, giving a ratio of 1 sarcoma to 66 carcinomas. At the Louisville General Hospital 2.0 per cent of all uterine malignancies were due to sarcoma and the ratio of sarcoma to carcinoma was 1:49.

TABLE II. COMPARATIVE INCIDENCE OF SARCOMA AS A MALIGNANT TUMOR OF THE UTERUS

AUTHOR	NO. CASES	PERCENTAGE OF UTERINE MALIGNANCIES	RATIO TO CARCINOMA
Kimbrough[6]	43	3.2	1:30
Searight[7]	12	2.1	1:53
Randall[4]	39	6.3	1:15
Kardash[8]	10	1.7	1:57
Cohen[9]	16	2.6	1:38
Thornton[5]	24	1.5	1:66
Murray[10]	21	4.0	1:24
Fenton[11]	26	5.5	1:18
Louisville General Hospital	15	2.0	1:49

Table III shows the incidence of sarcomatous changes occurring in fibroids as reported by different authors, and again a wide variation is noted. Kimbrough[6] reported that 0.76 per cent of fibroids undergo sarcomatous changes, whereas Randall's[4] incidence was 0.19 per cent. In this study 0.26 per cent of fibroids removed showed sarcomatous changes.

TABLE III. COMPARATIVE INCIDENCE OF SARCOMA OCCURRING IN MYOMAS

AUTHOR	TOTAL CASES	SECONDARY SARCOMAS	PERCENTAGE OF MYOMAS DEVELOPING SARCOMA
Kimbrough[6]	43	26	0.76
Novak[12]	51	39	0.52
Randall[4]	39	7	0.19
Kardash[8]	10	7	0.48
Fenton[11]	26	12	0.33
Finn[13]	33	16	0.30
Louisville General Hospital	15	9	0.26

Clinical Characteristics

Age.—The ages ranged from 35 to 84 years, the average age being 52 years. The highest incidence occurred in the fifth decade of life, and 80 per cent of the patients were over 40 years of age. There were no sarcomas in children. The age distribution was as follows:

30 to 39 years	3
40 to 49 years	5
50 to 59 years	3
60 to 69 years	2
70 to 79 years	1
80 to 89 years	1

Race.—Fourteen, or 93 per cent, of the cases occurred in Negroes. This is probably explained by the high percentage of Negro patients seen at this institution, as well as the greater incidence of fibroids seen in Negro patients.

Age at Puberty and Menopause.—The age at onset of menarche was between 12 and 14 years in 70 per cent of these patients. Nine, or 60 per cent, of the patients were postmenopausal and the average age at menopause was 46.5 years.

Marital Status and Parity.—All of the patients were married and 40 per cent had borne 3 or more children.

Symptoms.—The presence of an abdominal mass, abdominal or pelvic pain, and abnormal bleeding were the outstanding symptoms. Thirteen, or 86 per cent, of the patients noted the presence of an abdominal mass. Fifty per cent of those in the premenopausal group and almost 50 per cent of those in the postmenopausal group had abnormal bleeding. Pain is a late symptom and occurred in 66 per cent of these patients. A foul vaginal discharge was noted by all 3 patients with endometrial sarcoma.

Duration of Symptoms.—Nine, or 60 per cent, of the patients had symptoms of less than 6 months' duration and 5 of these gave a history of symptoms for less than 3 months. All patients who gave a history of symptoms of more than 24 months' duration had secondary growths, i.e., sarcomas which had developed in fibroids.

Size of Uterus.—The chief physical sign was enlargement of the uterus. In 11 cases, or 73 per cent, the uterus was enlarged to the level of, or above, the umbilicus.

Origin and Classification

Concerning the histogenesis of sarcoma of the uterus, it should be remembered that all the constituent elements of the uterus, i.e., muscle, connective tissue, epithelium, and blood vessels are derived from the mesoderm. The actual cellular origin is probably from undifferentiated mesenchymatous cells which are capable of developing into either smooth-muscle cells or fibroblasts, rather than from the differentiated cellular elements of the uterus.

TABLE IV. CLASSIFICATION

	SITE OF ORIGIN				
	PRIMARY				
CELL TYPE	ENDOMETRIUM	MYOMETRIUM	UNCLASSIFIED	SECONDARY	TOTAL
Spindle	1	2	1	6	10
Round					0
Mixed	2			1	3
Giant				2	2
Total	3	2	1	9	15

An attempt was made to classify these cases both as to the site of origin and as to the dominant type of neoplastic cell (Table IV). Six, or 40 per cent, of the cases were classified as primary sarcomas. The criteria for the diagnosis of primary tumors was the absence of gross or histological evidences of pre-existing myoma at the site of the sarcoma, or the absence of other myomas in the uterus. The primary tumors were further classified as to origin in the myometrium or endometrium, and this at times is very difficult to determine.

Three of the primary tumors were classified as endometrial in origin, 2 as myometrial in origin, and the origin of the remaining case was impossible to determine. This difficulty in determining the origin has led many authors to emphasize a classification based on the dominant type of neoplastic cell. Grouping our cases in this manner we found 10 cases of the spindle-cell variety, 3 cases of the mixed-cell variety, 2 cases of the giant-cell type, and no cases of the round-cell type.

Diagnosis and Treatment

In 10, or 66 per cent, of the cases in this series, the preoperative diagnosis was leiomyoma of the uterus. In 1 case the preoperative diagnosis was "uterine polyp." In 3 cases the diagnosis of sarcoma was made by biopsy of a polypoid mass protruding through the cervix. These 3 patients all exhibited a hard, nodular mass filling the pelvis and lower abdomen, and 2 of the 3 patients lived less than one month after biopsy. In 1 case the diagnosis was made by means of a diagnostic dilatation and curettage.

The method of treatment and 5-year survival are recorded in Table V. Failure to make the diagnosis preoperatively and at the time of operation accounts for the absence of deliberate planned treatment in most cases. Two cases of secondary sarcoma were treated by subtotal hysterectomy. One of these patients received postoperative deep x-ray therapy and is alive and well more than five years after treatment. No follow-up could be obtained on the other patient. Four cases were treated by subtotal hysterectomy and bilateral salpingo-oophorectomy. One of these patients with a secondary sarcoma is alive and well more than ten years postoperatively, while 2 others who also had a secondary type of sarcoma lived less than six months after operation. The fourth patient had a primary type of sarcoma and was given postoperative deep x-ray therapy but died five months after operation. One case was treated by total hysterectomy and unilateral salpingo-oophorectomy. This patient had a secondary type of sarcoma and is alive and well eighteen months after operation. Two cases were treated by total hysterectomy and bilateral salpingo-oophorectomy. One of these was classified as a primary sarcoma and the other as a secondary sarcoma, but both patients were dead within four months after operation. Treatment in one case consisted of myomectomy alone and this patient died two months after operation. One patient received radium implantation following local removal of a "polypoid tumor in the cervical canal." Adequate follow-up could not be obtained on this patient. One case occurring in an 84-year-old patient received only irradiation therapy because of the poor operative risk. The diagnosis was made by diagnostic dilatation and curettage and this patient lived less than six months after treatment. Three cases were considered inoperable and received no treatment. In these cases the diagnosis was established by biopsy and, as stated previously, 2 of the 3 patients lived less than one month after biopsy.

Two of the 12 patients who underwent an operation of some type (3 patients had biopsy only) died during the immediate postoperative period. One patient with a secondary type of sarcoma died of a pulmonary embolus on the

ninth postoperative day. The other death occurred in the operating room due to hemorrhagic shock. This patient had a primary type of sarcoma with widespread metastases to the liver, omentum, peritoneum, large and small bowels, and should probably have been regarded as "not resectable." These 2 deaths after 12 operations constitute an operative mortality of 16.6 per cent.

TABLE V. TREATMENT AND FIVE-YEAR SURVIVAL

PROCEDURE	NO. CASES	TYPE OF SARCOMA		FIVE-YEAR SURVIVALS
		PRIMARY	SECONDARY	
Subtotal hysterectomy	2		2	1*†
Subtotal hysterectomy with bilateral salpingo-oophorectomy	4	1†	3	1 (Secondary)
Panhysterectomy with right salpingo-oophorectomy	1		1	0
Panhysterectomy with bilateral salpingo-oophorectomy	2	1	1	0
Hysteromyomectomy	1		1	0
Local removal followed by radium	1		1	0*
Diagnostic dilatation and curettage followed by radium	1	1		0
Biopsy only	3	3		0
Total	15	6	9	2‡

*Result unknown in 1 case.
†Given postoperative deep x-ray therapy.
‡End result known in 13 cases only.

End Results

Adequate follow-up studies were obtained on 13 of the 15 patients in this series (Table VI). Only 2 patients are alive and well more than five years after treatment. A third patient is living and well eighteen months postoperatively. All 3 of the patients living had a secondary type of sarcoma, i.e., originating in a fibroid. Follow-up was obtained in all cases classified as primary type of sarcoma and all of these patients died. Nine of the 10 patients who died were dead within eight months after a diagnosis of sarcoma was made.

TABLE VI. END RESULTS

	PATIENTS	
	NO.	PER CENT
Cases with known end result	13	100.0
Alive and well 5 or more years	2	15.4
Alive and well 18 months	1	7.7
Operative mortality	2	15.4
Died of sarcoma	8	61.5
Within 6 months	6	
Within 8 months	1	
Within 30 months	1	

A comparison of the five-year survival rate as reported by different authors is listed in Table VII. This varies from an 8 per cent five-year cure reported by Thornton[5] to a 36 per cent five-year cure reported by Fenton.[11] Our five-year survival rate is 15 per cent.

TABLE VII. COMPARATIVE FIVE-YEAR SURVIVAL

AUTHOR	NO. OF SARCOMAS WITH FOLLOW-UP	FIVE-YEAR SURVIVAL	
		NO.	PER CENT
Kimbrough[6]	35	12	34
Novak and Anderson[12]	50	15	30
Randall[4]	29	9	31
Finn[13]	33	7	21
Thornton[5]	12	1	8
Fenton[11]	22	8	36
Louisville General Hospital	13	2	15

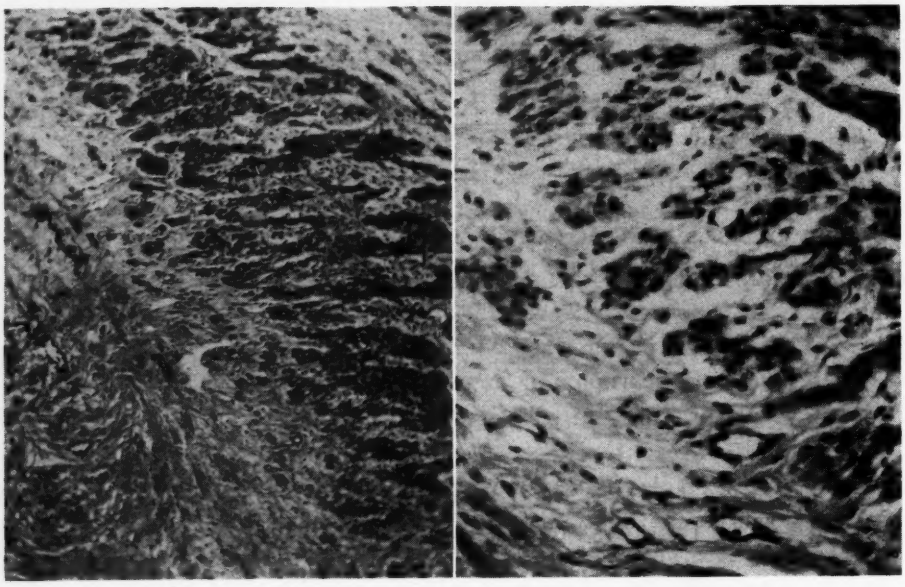
Comment

The variation in the reported incidence of sarcoma of the uterus as well as in the survival rate, may in part be accounted for by differences in the criteria upon which different observers have based their diagnoses. The main difficulty encountered is distinguishing between myomas showing atypical cellularity and myomas showing true sarcomatous changes. Some writers, such as Evans,[14] Kimbrough,[6] and Novak and Anderson,[12] have stressed the importance of the relative number of mitoses which may be present as an index of the degree of clinical malignancy. Evans[14] and Novak and Anderson[12] performed actual mitosis counts. Mitosis may vary from time to time in the same tumor, and certainly does vary in different parts of the same tumor, depending upon the degree of growth. In fast-growing myomas, sarcoma should be suspected, but the criteria for diagnosis should be infiltration and destructive growth rather than increased cellularity and mitosis.

The inclusion of doubtful cases for statistical purposes results in a higher incidence, a better survival rate, and, perhaps, a false impression of the possible seriousness of this tumor. In this study there were 2 cases in which a false positive diagnosis was made. These 2 cases were reclassified as cellular leiomyomas and not included for statistical purposes. Condensed histories and pathological illustrations of the 3 surviving patients are presented.

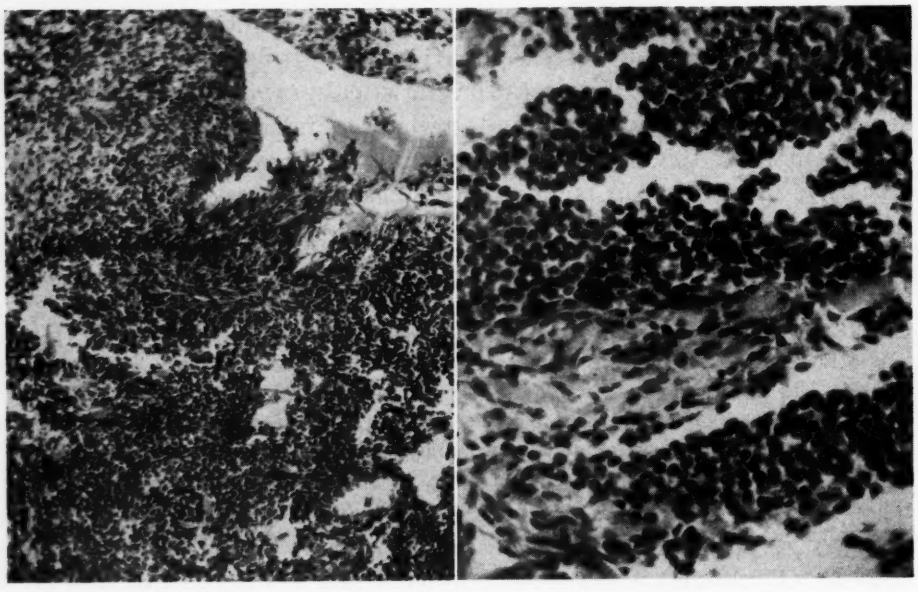
CASE 1.—(No. 62915) A 49-year-old gravida i, para i, was admitted Nov. 2, 1940. Her chief complaint was a gradually increasing mass in the lower abdomen for the past 5 years associated with irregular bleeding over the same period. A firm mass was found to be filling the lower abdomen extending to the umbilicus. The preoperative diagnosis was fibroid uterus. The operative diagnosis was fibroid uterus. The operation, subtotal hysterectomy and bilateral salpingo-oophorectomy, was performed on Nov. 4, 1940. The pathological diagnosis was leiomyosarcoma (Fig. 1) confined to a single, large leiomyoma. Follow-up in April, 1951, ten and one-half years after operation, showed the patient to be in good health.

CASE 2.—(No. 109444) A 38-year-old gravida ii, para ii, was admitted June 17, 1946. Her chief complaint was pain in the lower abdomen for the past 2 weeks. A soft mass was found in the lower abdomen extending to the umbilicus. The preoperative diagnosis was fibroid uterus. The operative diagnosis was fibroid uterus with probable degeneration. The operation, a subtotal hysterectomy, was performed on June 20, 1946. The pathological diagnosis was leiomyosarcoma (Fig. 2) with invasion of the myometrium. The patient was given irradiation therapy postoperatively and completed 7,200 r to four external ports on Aug. 1, 1946. Follow-up in December, 1951, five and one-half years after operation, showed the patient to be in good health.



A. *B.*

Fig. 1 (Case 1).—Secondary leiomyosarcoma. Patient alive and well ten and one-half years after treatment.
A, ×100, reduced one-sixth.
B, ×450, reduced one-sixth.



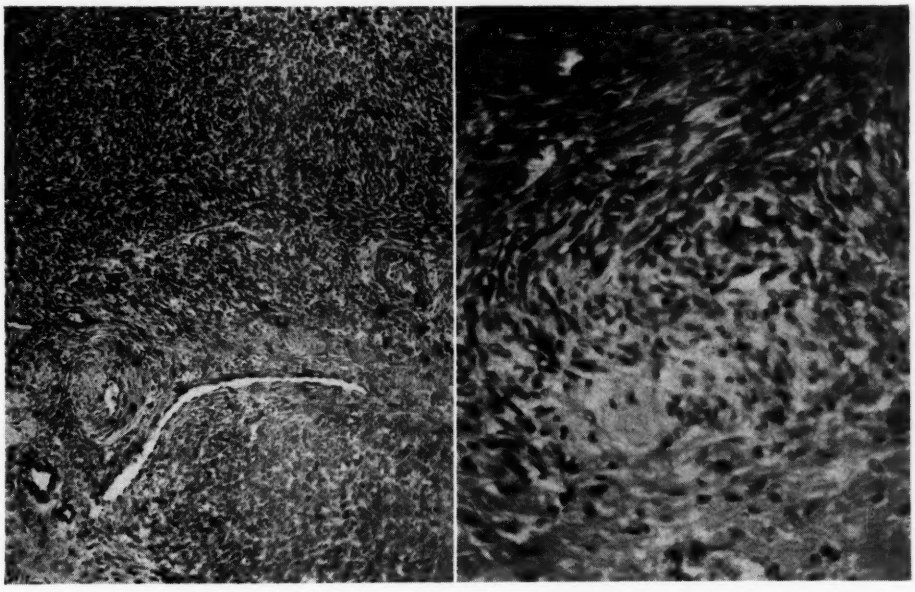
A. *B.*

Fig. 2 (Case 2).—Secondary leiomyosarcoma. Patient alive and well five and one-half years after treatment.
A, ×100, reduced one-sixth.
B, ×450, reduced one-sixth.

CASE 3.—(No. 208138) A 40-year-old gravida i, para i, was admitted Dec. 8, 1950. Her chief complaint was irregular bleeding for 6 months. The uterus was enlarged to the size of a 3 months' pregnancy. The preoperative diagnosis was fibroid uterus. The opera-

tive diagnosis was fibroid uterus. The operation, total hysterectomy and right salpingo-oophorectomy, was performed on Dec. 13, 1950. Pathological diagnosis: *gross* (Fig. 3); "The uterus measured 15 cm. by 12 cm. by 8 cm. The corpus was distended symmetrically, and over the serosal surface there were several firm nodules measuring from 1.5 cm. to 3.5 cm.

Fig. 3 (Case 3).—Secondary leiomyosarcoma. Patient alive and well eighteen months after treatment.



A. *B.*

Fig. 4 (Case 3).—Spindle-cell leiomyosarcoma with invasion of the myometrium.
A, ×100, reduced one-sixth.
B, ×450, reduced one-sixth.

in diameter. On cut surface the anterior wall of the myometrium was distended to a diameter of 6 cm. by a partially cystic mass which encroached upon the endometrial cavity but did not enter it. The cystic area was multiloculated, had a smooth serous lining, and

contained a slightly hemorrhagic, watery fluid. The cystic mass was indefinitely encapsulated and in areas there was no demarcation from the myometrial wall''; *microscopic* (Fig 4), ''leiomyosarcoma with invasion of the myometrium.'' She received no further treatment. Follow-up on Aug. 1, 1952, one and one-half years after operation, showed the patient to be in good health.

The symptoms and pelvic findings in sarcoma of the uterus usually lead to a preoperative diagnosis of leiomyoma. Growth more rapid than ordinarily noted in benign tumors or rapid increase in the size of a pre-existing myoma, especially when accompanied by abnormal bleeding, should, however, suggest sarcoma.

When the endometrial surface or the cervix is involved, cytological smears, diagnostic curettage, and cervical biopsy are helpful in diagnosis. Finn[13] was able to diagnose sarcoma correctly in 7 of 9 cases in which cytological smears were obtained. Five cases of endometrial sarcoma and 2 cases of secondary sarcoma which had invaded the endometrium exfoliated sufficiently to be recognized by cytological methods. The 2 false negative reports occurred in patients with secondary sarcomas which did not shed cells into the endometrial cavity. Routine cytological studies on all patients would undoubtedly lead to an earlier diagnosis and an increase in curability of endometrial and cervical sarcoma. The 3 patients in this series with endometrial sarcoma all had far-advanced cases when seen for the first time and none survived. There were no cases of sarcoma of the cervix.

Autopsies were performed on 2 patients in this series and both had metastases in the lungs and liver. Because the lungs are a common site of metastasis, Thornton[5] suggests a preoperative chest x-ray on all patients with myomas. This may prevent the embarrassment of a ''postoperative'' diagnosis.

Complete surgical removal is the most effective treatment for sarcoma of the uterus. However, because of the difficulties of diagnosis, a large proportion of sarcomas are not discovered until operation for supposed myomas, or until the pathological examination in the laboratory. The possibility of sarcoma should always be borne in mind by the surgeon, and it is wise to open the specimen immediately upon removal in the operating room. A presumptive diagnosis of sarcoma can sometimes be made from the gross appearance of the cut surface, and, if there is some doubt, a frozen section can be obtained. If sarcoma is found, a total hysterectomy and bilateral salpingo-oophorectomy should be performed. The 2 patients in this series who have survived more than 5 years were both treated by subtotal hysterectomy. However, both of these patients had comparatively early secondary growths which were completely removed by the subtotal operation. Two other patients with secondary sarcomas treated by subtotal hysterectomy died of recurrences in the cervix. It is regrettable that two-thirds of the hysterectomies in this series were subtotal. Our present policy of performing a total hysterectomy where hysterectomy is indicated for any cause whatsoever will probably result in a higher cure rate of sarcoma.

All surviving patients in this series had secondary sarcomas, whereas all patients with primary growths died within eight months after diagnosis. It is

evident that primary sarcomas grow and metastasize more rapidly than those arising in myomas and are relatively more malignant.

The value of radiotherapy is difficult to assess in this series; however, most writers doubt the efficacy of this form of treatment.[5, 10, 13] The postoperative use of deep x-ray therapy in one patient with secondary sarcoma confined to the uterus was probably unnecessary. Its postoperative use in another patient with primary sarcoma and omental metastasis at the time of operation was of no value, the patient surviving only five months.

Patients with advanced cases are poor operative risks as evidenced by the death of one patient on the operating table due to hemorrhagic shock. If the pathological diagnosis is made in such advanced cases, palliative irradiation rather than extensive surgery should probably be used.

Summary

1. A review of 15 cases of sarcoma of the uterus which occurred at the Louisville General Hospital during the period 1927 through 1950 is presented.

2. These 15 cases represented 2 per cent of all uterine malignancies seen during this period, and a relationship of sarcoma to carcinoma of 1 to 49.

3. The incidence of sarcomatous change in myomas was found to be 0.26 per cent.

4. The symptoms are not specific; however, pain, abnormal bleeding, and rapid enlargement of the uterus should suggest sarcoma.

5. Surgical removal is the accepted treatment, radiotherapy being of doubtful benefit.

6. The five-year survival rate was 15 per cent.

7. In our experience, true sarcoma of the uterus is an uncommon but highly fatal disease.

8. Suggested means of increasing the cure rate are (a) early diagnosis by routine cytological studies, (b) alertness to the possibility of sarcoma, both clinically and in the operating room, and (c) performance of total hysterectomy whenever hysterectomy is indicated for any reason.

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THE SPIRAL TWIST OF THE NORMAL UMBILICAL CORD IN TWINS AND IN SINGLETONS*

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OF ALL the characteristics of the human umbilical cord, one of the most obvious is the twisted or spiral course of its component blood vessels. This twist is perhaps "one of the less important but rather intriguing examples of the inscrutable in nature"[1] that "has been much and very unprofitably discussed."[2] It is the purpose of this paper to present new data and a new theory, as well as to review the relevant literature.

According to Lewis[3] the spiral course of the umbilical vessels in the cord was noted at least as early as 1521 by Berengarius[4] and was confirmed by Columbus[5] in 1559 and by Arantius[6] in 1564. Fabricius[7] in 1600 and his pupil Casserius[8] in 1626 showed in pictures that both dextral and sinistral spirals occur.

Dextral and Sinistral Spirals

To avoid confusion, it will be necessary to review certain facts. Mathematically speaking, the vessels of the cord are wound as cylindrical helices rather than as spirals, for a cylindrical helix remains equidistant from its central axis and retains a constant curvature, while a spiral recedes continually from its central axis, simultaneously decreasing its curvature.[9] Yet the term "spiral" is commonly used to include helices, and is so used in this paper.

In a dextral spiral (or in a dextral helix) held vertically, the portions of the spiral lying between the axis and the observer—or, as the observer might say, "in front of the axis"—will appear to slant from a point above on the right to a point below on the left. In a sinistral spiral so held, the reverse will appear; the anterior parts of the spiral will course from left above to right below. In other words, the course of the anterior portion of a dextral spiral will parallel the right-hand limb of a letter *V*, while the course of the corresponding portions of a sinistral spiral will parallel the left-hand limb of a letter *V*. This will be true no matter in which position a spiral is held for consideration. A left-hand screw will be a left-hand screw whether it is driven into a ceiling or into a floor. The spirality of an umbilical cord is the same whether it be oriented with respect to the fetal or the placental end, or whether it be regarded as an independent object.

To return to our practical example, note that if two long screw drivers were fixed together handle to handle, pointing one up and the other down,

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the same twist that would drive a right-hand screw into a ceiling would simultaneously drive a left-hand screw into a floor. An understanding of this paradox is essential for comprehension of my theory of the origin of the twist of the umbilical cord.

Direction and Amount of Twist of the Umbilical Cord

The umbilical cord is most commonly twisted in sinistral manner. The findings of Hunter,[10] Meckel,[11] Velpeau,[12] Neugebauer,[13] Read,[14] Hyrtl,[15] and Shordania[16] relevant to this point are summarized in Table I, from which it would appear that at least three-fourths of all cords have a sinistral twist.

TABLE I. DIRECTION OF TWIST OF UMBILICAL CORD

REFERENCE	TOTAL CASES	SINISTRAL TWIST	DEXTRAL TWIST	NIL TWIST	COMPLICATED DEXTRAL-SINISTRAL	PERCENTAGE INCIDENCE SINISTRAL TWIST
Hunter[10]	32	28	4	–	–	87.5
Meckel[11]	–	–	–	–	–	90.0
Velpeau[12]	–	–	–	–	–	83.4
Neugebauer[13]	160	114	39	7	–	71.4
Read[14]	54	42	8	3	1	79.4
Hyrtl[15]	120	86	15	3	16	82.6
Shordania[16]	199	105	94	–	–	50.3
Present author's singleton series	100	82	12	6	–	82.0

In 100 consecutive cords I examined, the major twist was sinistral in 82 and dextral in 12. In six of the cases the cord was straight, or else had an equal number of twists in each direction. The observed incidence of sinistrality is therefore 82 per cent.

Cords are not infrequently found in which different directions of twist occur in different segments. Indeed, reversals of twist may occur several times in the same cord, while straight segments may intervene between portions that are twisted. While mentioning this complication, Hunter[10] classified his cords simply according to the predominant twist. Neugebauer[13] also noticed the presence of straight areas intervening between the twisted segments, in 60 out of 153 cords. Of these 60 cords, the straight zone lay toward the fetal end of the cord in 41 instances, toward the placental end in 15, and occupied a middle position in 4. Among 120 cords that he studied, Hyrtl[15] described 16 as "complicated" in that they showed various combinations of sinistral, dextral, or nontwisted arrangements of the vessels of each cord.

The number of spiral turns per cord is also variable, as Hunter[10] noted. Neugebauer's[13] cords had from one-fourth to 41 twists. Hyrtl's[15] cases ranged from 0 to 36 twists. Shordania[16] found an average of 11 turns per cord in a series of 160 cords, with a range from 0 to 22 turns.

There is considerable variation in the length of the umbilical cord. A simple rule of thumb proposed by Leonardo da Vinci[17] is, "the length of the umbilical cord is equal to the length of the child in every stage of its age."

Winckel[18] gave the following ranges of cord length in relation to period of gestation:

6th week	5 mm.
4th month	16-18 cm.
5th month	22-30 cm.
6th month	33-35 cm.
7th month	37-40 cm.
8th month	42-45 cm.
9th month	46-49 cm.
10th month	50-52 cm.

Grosser[19] noted that while the cord is normally about the same length as the child, it may be reduced to almost nothing, or it may reach 3 times its normal length. Shordania[16] found an average length of 60 cm. in a series of 421 cords, with a range from 35 to 104 cm. Fog[20] reported an average cord length of 54.8 cm. for 1,467 premature infants, and an average cord length of 60.7 cm. for 6,533 infants at term, with a general average of 59.6 cm. for the 8,000 cases in his combined series.

Neugebauer[13] showed that longer cords tend to have a greater number of twists than do shorter cords. This was confirmed by Shordania,[16] who found a coefficient $r = + 0.56$ for the correlation of length of cord and number of turns, as computed from his series.

Hyrtl[15] demonstrated that the longer cords are also the ones in which reversals of direction of twist more commonly occur.

Hunter[10] and almost all subsequent observers, including myself, have noticed that cords tend to have more spiral turns toward the fetal end than toward the placental end.

The Index of Twist

For convenience, the ratio of the number of twists to the length of the cord may serve to express quantitatively the intensity and resultant direction of twist in a given cord. Since, in consideration of resultant direction, one dextral turn will counterbalance one sinistral turn, it will be reasonable to assign positive and negative signs to the ratios corresponding to the two directions of twist. In the present study, sinistral twists (the predominant type) are assigned positive values, while dextral twists are recorded as negative numbers. To give it a specific meaning, the ratio is expressed in terms of twists per 10 cm. of cord length. For example, a cord 40 cm. long, twisted sinistrally one turn, then straight, then twisted dextrally three turns, may be said to have a resultant twist, or index of twist, of −0.50 per 10 cm.

Three sources of error may be considered. First, cords are usually studied after the child has been detached together with a variable length of cord. The amount of cord so lost will be reasonably standard in any given hospital, and may be neglected because of this constancy. Second, fractional turns occur. Twists need scarcely be recorded with greater accuracy than to the nearest half turn. Third, there may be occasional difficulty in deciding what constitutes a turn, for strictly speaking it is the *vessels* that are twisted about

the central axis of the cord, rather than a simple twisting of the cord as a whole, and in some instances there are discrepancies in the twists of the umbilical vein and of the two umbilical arteries. Usually the two arteries follow one another regularly. In cords where deviation from this rule has occurred, I have recorded quantitative twist according to the count of the turns made by the most prominent artery.

My quantitative data on twist of the cord in 100 consecutive cases of singleton pregnancy are presented graphically in Fig. 1. The mean length of cord in this series is 43.85 cm., and the mean index of twist (pooling all values of twist index without regard to direction of twist) is 1.56. The 82 sinistral cords in the series have a mean index of twist of 1.71, while the 12 dextral cords have a mean index of twist of − 1.25. The remaining 6 cords have no resultant twist, so their mean index of twist is 0.

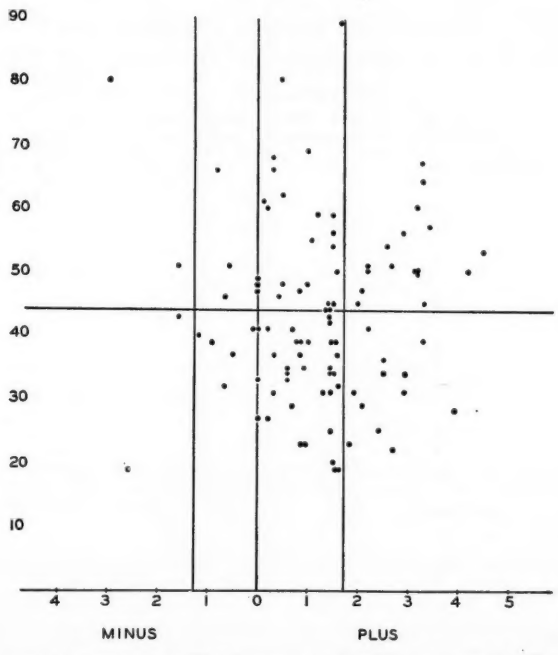

Fig. 1.—Length and twist in singleton cords . Length of umbilical cord, in centimeters, is plotted along the vertical axis while index of twist, in turns per 10 cm., is plotted along the horizontal axis. The vertical lines parallel to the line of zero twist mark the mean indices for plus (or sinistral) twists and minus (or dextral) twists. The horizontal line indicates mean length of all cords. Compare with Fig. 2.

Twist of the Umbilical Cord in Twins

Despite the great number of studies of twins and of twin placentas, very few observations have been published relative to the umbilical cords of twins. Hyrtl's[15] series of placentas included 32 pairs from twins. The cords that accompanied these placentas were figured and described without indication that they differed in any significant manner from the cords of the singleton placentas.

Qualitative data on the present series of fifty pairs of twin placentas (a consecutive series obtained from two hospitals, augmented by two monoam-

niotic cases from another source) are summarized in Table II. A first glance at this table might suggest that reversal of twist is unusually common in twins, since in only 27 *pairs* of the series of 50 pairs were both cords twisted in the predominant (sinistral) manner. Such a conclusion, however, would be incorrect. Each pair includes two individuals, and hence there is a sinistral cord as well as a dextral cord in each of the pairs classified in the "sinistral-dextral" column. This leads to consideration of the twin cords as *individual* cases, rather than as pairs. As recorded in the lower portion of Table II, there were 74 sinistral cords, 18 dextral cords, and 8 parallel cords, among the 100 twin individuals. Viewed statistically, this fails to differ significantly from numbers in the observed nontwin population, as differences between the twin and singleton series (in respect to direction of twist) are in no case as great as twice the standard error of the difference.

TABLE II. DIRECTION OF TWIST OF UMBILICAL CORD IN TWINS

	BOTH SINISTRAL	ONE SINISTRAL ONE NOT TWISTED	BOTH NOT TWISTED	ONE DEXTRAL, ONE SINISTRAL	BOTH DEXTRAL	TOTAL
A. Cords Considered as Pairs.—						
Type of placenta:						
Dichorionic, separate	14	2	1	4	1	22
Dichorionic, partially fused	4	0	0	5	0	9
Dichorionic completely fused	6	1	0	5	0	12
Monochorionic	3	1	1	2	0	7
Sex of twins:						
Male-male	9	1	0	5	1	16
Male-female	11	1	1	6	0	19
Female-female	7	2	1	5	0	15
Total *pairs* of cords	27	4	2	16	1	50
B. Cords Considered as Individuals.—						
Individual cord twist:						
Sinistral	54	4	0	16	0	74
Dextral	0	0	0	16	2	18
Not twisted	0	4	4	0	0	8
Total *individual* cords	54	8	4	32	2	100

This is of interest in view of the belief restated by Newman[21] (and commonly voiced by others) that there exists a tendency for "mirror-imaging" of asymmetrical physical traits in twins, especially in those of monochorionic type. Price,[22] on the contrary, recently doubted that there had been a convincing demonstration of greater frequency of lateral inversions in monochorial twins than in dichorial twins (though he expected a greater frequency, from theoretical considerations). Torgersen[23] has recently shown that twins are no more common in a large series of cases of major situs inversus of viscera than they are in the general population.

Whatever the cause may be for the normal preponderant incidence of sinistral cords, it is not significantly altered by cleavage or multiplicity of the ovum.

Schatz,[24] concerned with the disparity in weight or size between members of the monozygotic twin pairs which he studied in relation to the character of intraplacental anastomoses between the circulatory systems of the members of the respective pairs, claimed that the "favored" twin shows greater twist of the vessels in his umbilical cord than does the co-twin. He supported this belief by reference to drawings of vascular injections of several pairs of placentas, in which one cord of each pair appears more twisted than its mate.

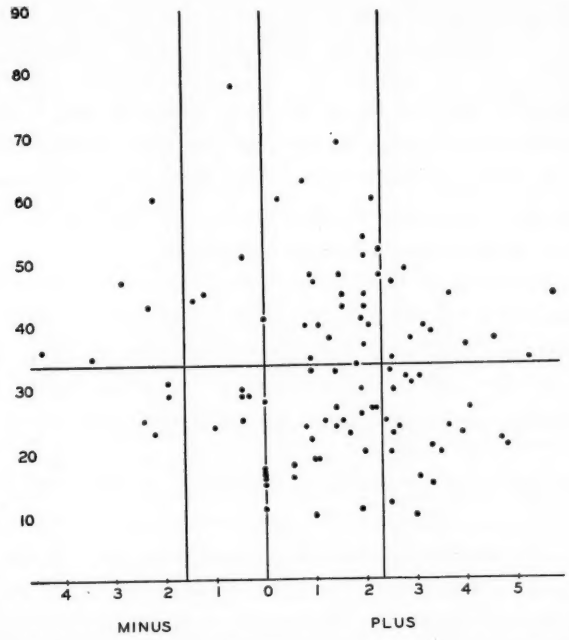

Fig. 2.—Length and twist in twin cords. Mean length of cords and mean indices of twist are indicated as in Fig. 1. Note that these twin cords tend to be shorter and to have greater twist than the singleton cords plotted in Fig. 1.

The quantitative data on twist of the cords in my series of 100 twin individuals are presented in Fig. 2. The mean length of cord in this series is 33.70 cm., and the mean index of twist (pooling all values of twist index without regard to direction of twist) is 2.03. The 74 sinistral cords in the series have a mean index of twist of 2.32, while the 18 dextral cords have a mean index of twist of − 1.58. The remaining 8 cords have no resultant twist, so that their mean index of twist is 0.

When the distribution of twist indices for twin cords (Fig. 2) is compared with the distribution for singleton cords (Fig. 1), it is seen that the cords of the twins tend to be slightly shorter and rather more twisted. Differences between the twin series and the singleton series, in respect to mean cord length and mean index of twist, each exceed three times their standard errors, and are therefore statistically significant, as shown in Table III.

Dextral cords tend to be less twisted than sinistral cords, in both the twin and the singleton series. Though the differences between the mean indices of twist of the dextral cords and of the sinistral cords are not sta-

tistically significant in either the twin or singleton series, the trend suggests that some factor associated with the reversal of twist *direction* from sinistral to dextral may inhibit the *amount* of twist developed.

TABLE III. COMPARISON OF DATA IN THE SINGLETON AND TWIN SERIES

SINGLETONS		TWINS		DIFFERENCE	
Mean Length of Umbilical Cord.—					
43.85 cm.	14.25	33.70 cm.	13.65	10.15 cm.	0.197
Mean Index of Twist of Umbilical Cord.—					
1.56	1.08	2.03	1.30	0.47	0.017

That the observed greater twist of twin cords is not a simple correlate of the coincident shortness of these cords may be seen from both charts (Figs. 1 and 2). In neither series is there correlation between length and index of twist. In the twin series the computed coefficient is $r = 0.023$; in the singleton series $r = 0.084$. Neither value is statistically significant.

It is common knowledge that twins tend to be born prematurely. Can the factor of prematurity explain the greater twist of the twin cords? Reasonably reliable menstrual histories were available for most of the patients from whom were derived the 100 single placentas. Suitable tabulation shows no indication of correlation between duration of pregnancy and index of twist of cord.

Weight of the fetus is of course a correlate of duration of pregnancy, and therefore one would not expect it to show correlation with twist of the cord. Actually no such correlation is found. Similarly, sex of the fetus has no effect on the direction or amount of twist developed by the cord.

The twin placentas were studied with respect to site of implantation of the cord, and occurrence of circumvallate portions. No correlation could be found between direction or amount of twist of the cords and the distance between the placental insertions of the two cords, between twist and distance of the cords from the nearest placental margin, or between twist of cords and occurrence or extent of circumvallation of the placentas.

The direction and amount of twist of the two cords in each twin pair of the series is shown graphically in Figs. 3 and 4, constructed for the determination of intrapair correlation according to the method of Fisher.[25] In each of these figures there are two entries for the indices of any pair of cords. In a given pair, the index for cord *A* was plotted as abscissa against the index for cord *B* as ordinate, and then the index for *B* was plotted as abscissa against the index of *A* for ordinate. Indices of twist were plotted without regard to algebraic sign. Symbols were used to indicate whether the corresponding placentas were monochorionic, dichorionic fused, or dichorionic separate.

The group of pairs in which the two cords that comprised each set had the same direction of twist (Fig. 3) has a computed coefficient $r = 0.662$, indicating good intrapair correlation in respect to index of twist. The group of pairs in which the two cords of each set had opposite directions of twist (Fig. 4) has a coefficient $r = -0.090$, demonstrating a lack of significant intrapair correlation.

It is further shown in Fig. 3 that the good intrapair correlation in amount of twist, in the group of pairs with like direction of twist, is independent of the type of placenta—monochorionic or dichorionic. Since with one exception all of the pairs in this group of cords were sinistral-sinistral pairs, it may be presumed that the *amount* of twist of a cord is determined by factors independent of the conceptus itself, as long as the cord has the usual sinistral twist.

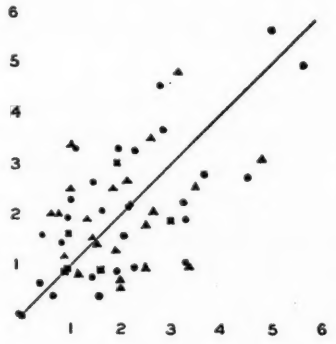

Fig. 3.—Intrapair correlation: Twin cords with the same direction of twist in the members of each pair. Index of twist of each cord in a pair is plotted against the index of twist of its mate, and vice versa, according to a method of Fisher.[25] Shape of dot indicates type of placentas (square = monochorionic, triangular = dichorionic fused, and round = dichorionic separate). Note tendency of plotted values to lie along the diagonal line of direct correlation. Compare with Fig. 4.

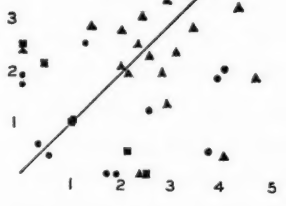

Fig. 4.—Lack of intrapair correlation: twin cords with opposite direction of twist in the members of each pair. Indices of twist are plotted according to the same method and using the same symbols as in Fig. 3. Note wide scatter of plotted values over the field, indicating lack of correlation. Compare with Fig. 3.

The lack of significant intrapair correlation in respect to amount of twist in the group of twin pairs that had mixed or sinistral-dextral cords demonstrated in Fig. 4 seems to indicate that there is something inherent in the reversal of the normal *direction* of the twist of the cord that lessens the *amount* of this twist.

Theories of the Origin of the Twist of the Umbilical Cord

Any theory purporting to explain the spiral structure of the normal umbilical cord may be expected to provide reasonable answers to the following questions:

1. Why do some cords show more twist than others?

2. Why is the twist more marked toward the fetal end of the cord than toward the placental end?

3. Why are some cords straight, and why have some cords a combination of dextral and sinistral twist?

4. Why does reversed or dextral twist occur with relative infrequency?

5. Why does reversed or dextral twist occur with the same incidence in multiple as in single pregnancy?

6. Why do the cords of twins tend to have greater twist than those of singletons?

Minot[2] considered the possibility that the vessels become twisted within the cord as within a sheath, because they are longer than the cord and must therefore be compressed in order to fit. He pointed out that the twisted appearance of the vessels does not necessarily indicate an actual twist of the cord as a whole, for "if a long rubber tube forms a coil within a short glass cylinder, it does not indicate that the cylinder has been twisted." Most writers, however, have treated the twist of the vessels in the cord as if it were synonymous with twist of the cord in its entirety.

The simplest explanation of the twist of the umbilical cord is that offered by Velpeau,[12] that the embryo itself induces the twist by active rotary motions produced by movements of the limbs. The intriguing picture of the young embryo swimming about in amniotic fluid is, however, obscured by the fact that active motions of the embryo do not occur during the period in which twists begin to form in the cord. The tendency for the cord to twist has been noted as early as the sixth week (embryos of 10 mm. length), according to Cullen[26] and is well established in the next few weeks. At two months, movements are quite uncoordinated, according to Minkowski.[27] Langworthy[28] and Hines and Boynton[29] also stress the late onset of neuromuscular activity.

Haller,[30] followed by Osiander,[31] Kilian,[32] Burdach,[33] and Allen[34] explained twist of the cord on the basis of the greater length of the umbilical arteries as compared to the vein. Such theories fail to account for direction of twist and are therefore not satisfying.

A hydrodynamic explanation was offered by Schroöder van der Kolk,[35] who argued that the embryo would tend to be driven obliquely away from its cord by the force of recoil, when it pumped blood toward the placenta. The direction of twist, according to this theory, depends on whether the umbilical arteries lie to the right or to the left of the umbilical vein, at the umbilicus. That such an asymmetry of the umbilical vessels does exist at a time when twists in the cord are forming is indicated by the embryological studies of Cullen.[26] The left umbilical vein usually persists, while the right umbilical vein atrophies. The umbilical arteries deviate toward the right, at the point of departure from the body. Data are not at hand, however, to indicate a reversal of this asymmetry in embryos with dextral (reversed) twist of the umbilical cord. To the contrary, the preponderance of the left umbilical vein

seems to be quite constant, according to Arey,[36] probably having been determined already in embryos of 5 mm. length by pre-existing asymmetries in the development of the liver and mid-gut. Visceral inversions are quite rare in comparison to reversals in direction of twist of the umbilical cord. Finally, the position theory of Schröder van der Kolk[35] fails to explain cords that display combinations of dextral and sinistral twist.

The importance of asymmetry in size of the umbilical arteries, rather than asymmetry in their position, was stressed by Simpson.[37] He held that the force of recoil from the right umbilical artery is greater than that from the left, as the right vessel is usually larger than the left. But I have encountered cords with dextral twist as well as ones with sinistral twist in association with infants showing preponderance of the right umbilical artery, as well as in the case of infants that have only one umbilical artery. For example, one of a pair of dichorionic opposite-sexed twins was found, on dissection, to have no right umbilical artery. The co-twin had both umbilical arteries, the right being slightly larger than the left. The umbilical cord of each of these twins had had sinistral twist. It may be added that an entirely straight cord has been encountered, having only one artery, and two straight cords have been seen, each having the usual two arteries. Such facts tend to discredit any theory of twist production dependent upon asymmetries of the umbilical arteries.

Another hydrodynamic theory was proposed by Neugebauer.[13] He believed that the blood pressure is greater in the umbilical vein than in the umbilical arteries. He further thought that the vein can lengthen only by twisting, and in so doing it twists the arteries with it. Neugebauer's explanation of the prevalence of sinistral twist as the result of preponderance of the right umbilical artery seems unacceptable, for reasons already stated.

Grosser[19] explains the twist as the result of unequal growth of the two umbilical arteries, associated with slight differences which exist in the diameters of these two vessels. Here again is a theory unable to deal with cords having but a single artery.

If the twist of the umbilical cord is not to be explained as the result of factors inherent in the cord itself, or inherent in the embryo, then this twist must be the result of factors external to the embryo and its adnexa. The twist must be imposed upon the embryo and cord as upon passive objects. Sellheim[38, 39] compares the mechanism involved to that which he considers responsible for the torsion of any intra-abdominal tumor upon its stalk. Any mobile, pedunculated tumor has inertia and momentum, and will therefore tend to move in a direction opposite to that in which the rest of the body moves, whenever the body initiates or terminates motion. The net results of the many motions made by a patient carrying an intra-abdominal stalked tumor (or an embryo) will be torsion of the tumor on its stalk (or torsion of the embryo on its umbilical cord). The direction and extent of the twist are determined, according to Sellheim[38, 39] by the position of the placental end

of the umbilical cord. Küstner[40] had previously claimed that tumors of the right ovary tend to show sinistral torsion, while tumors of the left ovary show dextral twisting of the pedicle. Unfortunately, data are not at hand to indicate whether or not dextrally wound cords are associated with implantations toward the left wall of the uterus. Existing studies of early implantations by Hertig[41] and by others show no preponderance of one side of the uterus over the other, yet there are many more sinistral cords than dextral ones.

Sellheim[39] reproduced a diagrammatic figure from Küstner[40] showing bilateral ovarian tumors, the stalk of the right twisted sinistrally, that of the left twisted dextrally. He stated that a similar situation may exist in the case of twin pregnancy, the two umbilical cords displaying twists of opposite direction when their sites of implantation are widely separated, simulating the conditions present in the case of bilateral ovarian tumors. Conversely, twin cords having implantations nearer one another would be expected, on this theory, to have the same direction of twist.

Mutel, Vermelin, and Dombray,[42] considering cords of singletons, proposed that the direction of twist of the cord is determined by the reciprocal relation of the position of the fetal and placental insertions of the cord. According to these authors, the placental insertion is usually higher than the fetal, and the cord has a sinistral twist. When the placental insertion is lower than the fetal, the cord has a dextral twist. But this claim is not supported by any data on position of cord insertions.

In the present series of fifty twin placentas, no relation could be found between direction of twist and site of placental insertion of the cords, as evidenced by the distances between the insertions and the placental margins. In one instance, the cords of a fused dichorionic placenta were implanted side by side in the middle of the placenta, yet one cord showed sinistral twist and the other dextral.

Although one may be skeptical of Sellheim's[38, 39] theory or of its modifications, on the basis of these observations, still one will agree that the embryo is particularly liable to torsion as the result of influences external to it.

The Problem of the So-Called "Twist Amputation"

The specimen shown in Fig. 5 is representative of a not uncommon problem that confronts the obstetrical pathologist. Here is a fetus with sitting height of 13.2 cm. and foot length of 1.8 cm., well formed, but showing early maceration with a break in the anterior abdominal wall that exposes coils of intestine. The umbilical cord is twisted sinistrally 23 turns in the first 27 cm. of its course away from the placenta (index of twist: 8.5) and in this portion maintains a diameter averaging 0.6 cm. One cm. away from its insertion into the fetus, the cord narrows abruptly into a stalk ranging from only 0.1 cm. to 0.2 cm. in diameter, twisted tightly into 6 sinistral turns.

Clinically, this conceptus constituted the fourth pregnancy of a 39-year-old woman. Catamenia occurred on December 22, and on April 16 following

the dead fetus was passed. Bleeding occurred in the three days preceding the abortion. The menstrual age of the fetus is 16 weeks, in good accord with the anatomical age of 17 weeks as estimated from the charts of Streeter.[43]

Did the extreme torsion of the fetal end of the umbilical cord occur before the death of this fetus, causing this death, or did torsion take place after death?

The older pathologists (literature reviewed by Schauta[44]) were inclined toward the former view. Schauta,[44] however, championed the latter theory, pointing out that no signs of congestion are found in fetuses associated with such acutely twisted cords—that such fetuses are not infarcted. This idea has found increasing acceptance. Hirst[45] remarked, "Most modern observers regard it [i.e., excessive torsion of the cord] as a postmortem occurrence resulting from the great mobility within the uterine cavity of a fetus that has died."

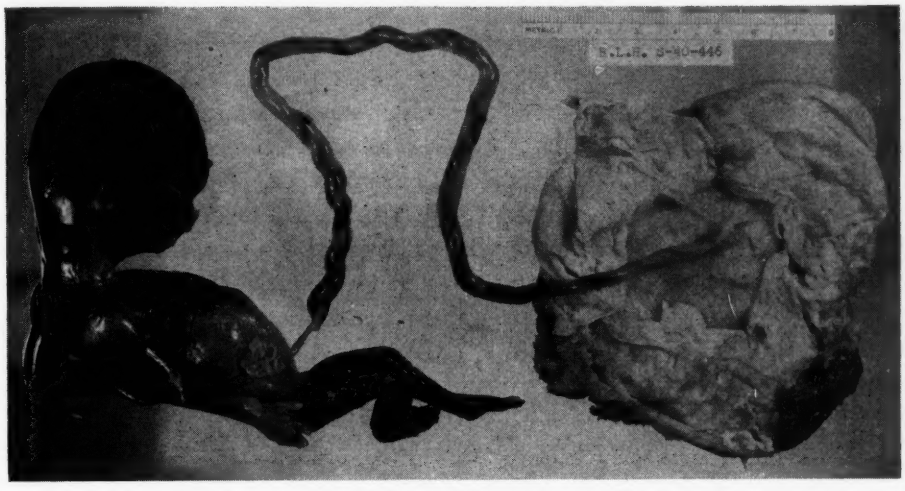

Fig. 5.—So-called "twist amputation." Extreme torsion of the fetal end of the umbilical cord is thought to arise *after* death of the fetus, and to result from the continuing action of the same extrinsic twist-producing factors that were present when the fetus was still alive.

The classic site of "twist amputation" of the umbilical cord is its fetal end, rather than its placental end. It is logical to assume that the localized thinning of the cord consequent on its overtwisting occurs in an area of relative weakness. Just such a zone of lessened tensile strength may be produced by necrobiosis, appearing first in the fetal end of the cord and progressing later to the placental end (end closest to the supply of oxygen, etc.). This may not be the only factor involved, because in the normal cord twisting tends to be greater at the fetal pole than at the placental, for reasons to be considered later.

Further evidence that stricture and overtwisting of the cord are sequelae and not precursors of fetal death is supplied by the common observation that in a series of miscarriage specimens the cords of the macerated fetuses tend to be more twisted than the cords of the nonmacerated ones.

As Eastman[46] stated the case, "As the result of movements on the part of the fetus, the cord may become more or less twisted . . . the most extreme degrees occur only after the death of the fetus. . . ." Such movements "on the part of the fetus" can be only pasisve. Twisting of the cord proceeds more extensively with the fetus dead than with the fetus alive, but in either instance it is most probably the same process, carried out by the same mechanisms.

A New Theory of the Cause of the Twisting of the Normal Umbilical Cord

For the reasons stated in the preceding sections, the twist is most probably imposed on the embryo and its cord as passive objects, by external forces. The theory of Sellheim,[38, 39] though directed in accord with such considerations, fails to explain such facts as the occasional opposite twist of twin cords having contiguous placental insertions.

As an alternate theory, it is here proposed that *the twist of the normal umbilical cord is the result of a rotatory movement imparted to the embryo by the asymmetrical contraction of the uterus.*

The contractility of the normal human uterus in late pregnancy is an accepted clinical fact. That the uterus contracts in somewhat similar fashion as early as the twenty-third week of pregnancy has been demonstrated by tocography (Murphy[47]). It seems probable that minor contractions, too small to be detected by means now available, may occur even during the first stages of pregnancy. Very slight contractions might impart a rotatory movement to the embryo, through the amniotic fluid, for the embryo is of little weight, balanced in the fluid.

The net effect of the contractions of the uterus may be expected to be asymmetric. Rarely if ever does the uterus lie exactly in the midline of the body. There is obvious asymmetry in the pressure of the uterus against adjoining viscera, for the rectum regularly enters the pelvis from the left. Too, there may be functional asymmetries in the uterus itself, for a spiral arrangement of muscle fibers in the uterus, dextral in the left half and sinistral in the right half of the organ, has been claimed by Fischer[48] and by Goerttler[49] and one or the other systems of muscle fibers may show slight functional predominance. *Asymmetric contractions* would result in net twist of the embryo and its cord in a fairly constant direction.

The avian egg bears evidences of comparable twist. The oviduct of a bird is highly asymmetrical, and includes in its wall muscle that may show some degree of spiral arrangement, as noted by Fischer[50] and by van den Broek.[51] The egg of a bird is twisted during its descent of the oviduct, and permanent traces of this torsion appear regularly in the chalazas of the albumin, and occasionally in minor textural markings of the shell, according to Romanoff and Romanoff,[52] and according to Conrad and Scott.[53]

One would expect variation in the amount of twist of umbilical cords, because variation in the degree of motility of the gravid uterus exists. An

attempt to correlate this mobility (as indicated by tocography) with the twist of the umbilical cord of the corresponding conceptus is suggested as an approach to this problem. Lacking such quantitative evidence, it may be pointed out that, as reported earlier in this paper, the umbilical cords of twins tend to be more twisted than the cords of singletons. The excess twist, not satisfactorily explained by the relative shortness of these twin cords, by the relative prematurity of the corresponding gestations, or by the relative underweight of the twins themselves, may perhaps be ascribed to the hypermotility of the uterus that, according to clinical experience, characterizes twin pregnancies.

The theory proposed here explains easily the good intrapair correlation of twin sets having sinistrally wound cords. The similarity is due to the common environment of the members of the pairs. Both embryos are subject to the torsion exerted by the same uterus.

Twist reversals or alterations in the direction of twist also find a simple explanation. The direction of twist of the cord will on this theory, be determined by the relation of the embryo and its cord to the effective axis of torsion of the uterus. In a given uterus, the twist put on the cord of an embryo directed upward from its placental insertion will be opposite in direction to the twist put on the cord of the same embryo directed downward from its insertion. If the truth of this statement is not apparent to the reader, he is referred to the preliminary discussion of spirals, in the first part of this paper.

Reversals of twist in any one cord are to be attributed to simple reversal in position of the embryo during the time in which the cord is liable to twist deformation.

If, on one hand, some 82 per cent of all cords display a net sinistral twist, then some 82 per cent of all embryos must occupy a certain net position with relation to the effective axis of torsion of the uterus. What this mean position of embryos may be lies beyond the province of this paper to discuss. Ideas held on this matter have been summarized in Eastman[46] and in other textbooks. A final solution of this problem might afford quantitative confirmation of my theory of the origin of the twist of the cord.

Dextrally wound cords are not encountered more frequently among breech presentations than among cephalic ones, nor might an increased incidence be expected, for mode of presentation is not necessarily an index of the position in early pregnancy, the time when the twists are applied to the cord.

Whatever the cause of the usual position of the embryo in early pregnancy, this factor must be only partly counteracted by the effects of multiple gestation. The absence of intrapair correlation in amount of twist of cords of sinistral-dextral pairs, commented on earlier as an indication that something inherent in the reversal of asymmetry interferes with the normal quantitative development of twisting, here finds an explanation. The reversal in *position* to which is attributed the reversal in cord twist is counteracted by

the factors tending to induce the normal position. This interaction of factors may result in placing the embryo in a relatively neutral position, that is, in one relatively transverse to the effective axis of torsion of the uterus, so that the quantitative development of twist will be diminished. Note that the invocation of hypothetical position factors does not imply active movement on the part of the embryo; indeed the factors may be purely mechanical, such as specific gravity, or conformation of shapes.

The trend toward lower index of twist in dextral cords than in sinistral ones, observed in both the singleton and twin series, can perhaps be explained in similar fashion.

It is proposed, then, that *the direction of the twist of the normal umbilical cord is determined by the position of the embryo in relation to the effective axis of torsion of the early gravid uterus.*

A Working Model for the Demonstration of the Mode of Production of the Twist of the Umbilical Cord

Speculations about the problems of twist of the umbilical cord may be facilitated by the use of the simple mechanical model shown in Figs. 6 and 7. The device consists of a small cardboard tag (representing an embryo) joined to a larger piece of cardboard (placenta) by three equal lengths of colored wool (vessels of the umbilical cord). If one places such a cardboard "placenta" flat on a table, and picks up the "embryo," the strands of wool will form a simple, untwisted "cord." If the "embryo" is now rotated on its long axis as one would rotate a screw driver to insert a right-hand screw into the "placenta," the "cord" will be found to undergo sinistral torsion.

As displayed in the figures, the "placentas" of two such units have been hinged together to represent a twin pregnancy. In Fig. 6, both of the "twin embryos" are oriented in the same direction. Both have been subjected to three complete turns—turns that would rotate a screw driver to insert a right-hand screw into the "placentas," and hence both cords display three complete sinistral twists. In Fig. 7, the model twins are oriented in opposite directions. Both have been subjected to the same torsion—nine complete turns, in the same direction as before. Here the *direction* of the twist is opposite in the two "cords," though the *amount* of the twist is the same. The "cord" directed up has a dextral twist, while the "cord" directed down bears a sinistral one.

The mechanical model demonstrates two additional facts about umbilical cords, both of which are evident in the illustrations. In Fig. 6 it may be noted that the two "cords" are more tightly twisted toward their "embryonal" ends than toward their "placental" ends. The length of "cord" occupied by the turn nearest the "placenta" is about one and one-half times the length of the turn nearest the "embryo." As noted previously, this increase in amount of twist, passing from placental end to fetal end, is characteristic of most, if not all, umbilical cords. A few trials with the model will convince one that this peculiarity has a simple mechanical explanation. Twists are added to the "cord" when the "embryo" is turned on its axis; they appear first at

the "embryonic" end of the "cord," while the "placental" end remains fixed. As more and more twists are added to the "cord," they slide along toward the "placenta."

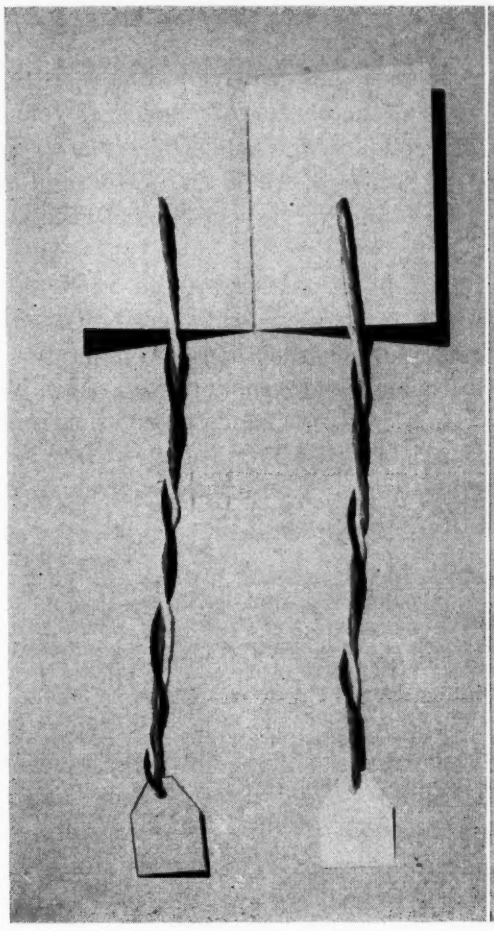

Fig. 6.

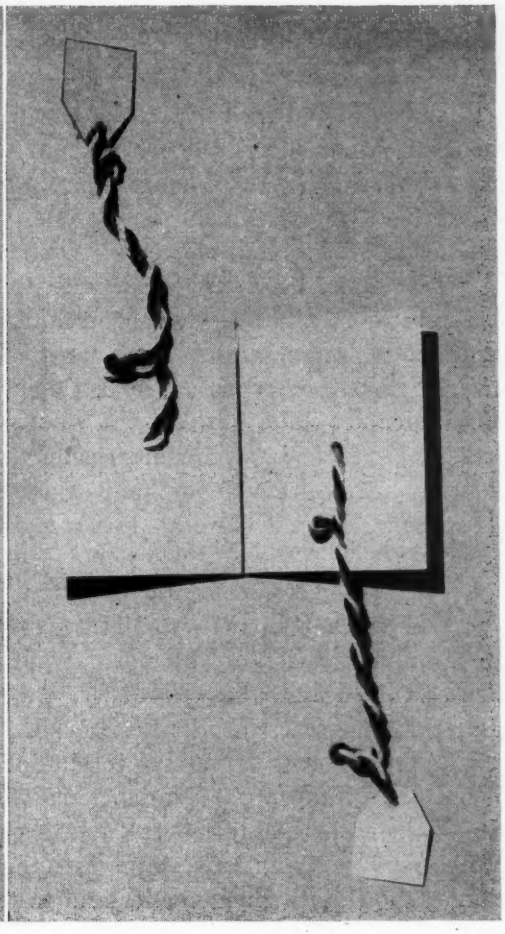

Fig. 7.

Fig. 6.—A mechanical model of twins, their cords and placentas. Similar orientation of the "twins" with respect to their "placentas" results in the same direction of twist of the "umbilical cords" when the same extrinsic torsion is applied to the "twins." Compare with Fig. 7.

Fig. 7.—A mechanical model of twins, their cords and placentas. Opposite orientation of the "twins" with respect to their "placentas" results in opposite direction of twist of the "umbilical cords" when the same extrinsic torsion is applied to the "twins." Compare with Fig. 6.

The model also offers an explanation of the so-called varices or false-knots—segments in an umbilical cord in which the vessels appear locally redundant, forming erratic accessory loops or tortuosities. Two such varices appear in each of the "cords" of Fig. 7. Two possible explanations summarized by Arey[36] are that the blood vessels curl in loops, "by stronger local growth, or perhaps, in part, by a local unwinding." The model affords evidence in favor of the second, or simple mechanical explanation. A few trials

with the model suffice to show that "varices" arise through the separation and subsequent kinking-up of the component strands of the "cord," or through kinking of the "cord" as a whole. Both processes supervene when the "cord" has become twisted to a certain degree, and are expressions of structural resistance of the strands to the twisting. Varix formation may entail a certain amount of absorption of twists. In human cords, the structural resistance of the component vessels would appear to be such that relatively little twisting will suffice to induce varix formation, and that the observed range of development of twists affords no significant differences in incidence of varices. In my series, one varix or more was noted in 26 of the 100 twin cords, and in 27 of the 100 cords from singletons. There was no correlation between incidence of varices and degree of twist.

The model may suggest answers to other questions. As noted by Neugebauer,[13] the straight sections sometimes found to intervene between the twisted sections of longer cords occur most often in cords that have been wrapped around the attached fetus, in the form of a loop. The model offers a simple mechanical explanation. If the wool strands of the twisted "cord" are subjected to gentle lateral compression, the twists will tend to move to the adjoining, uncompressed portions. Such migration of twists may well occur in a real cord, when it is wedged between fetus and amnion.

Résumé of Theories

The various theories that have been proposed to account for the origin of the spiral twist of the normal umbilical cord may be grouped into two classes. Theories that the twist is inherent in the cord itself: Minot,[2] Haller,[30] Osiander,[31] Kilian,[32] Burdach,[33] and Allen[34]; theories that the twist results from active or passive torsion of the embryo: Velpeau,[12] Schröder van der Kolk,[35] Simpson,[37] Neugebauer,[13] Sellheim,[38, 39] and myself. Most of the latter theories, including the one here proposed, involve relatively simple mechanical explanations, implying that the twist of the cord is quite incidental to its other properties and to its functions. My own theory is recommended as a simple one, in better accord with the known facts than is any other theory.

Conclusions

In a consecutive series of 100 umbilical cords from singleton pregnancies, the major twist was sinistral in 82, dextral in 12, and nil in 6. In a corresponding series of 50 pairs of umbilical cords from twin pregnancies, the major twist was sinistral in 74, dextral in 18, and nil in 8.

In these series, quantitative development of twist was greater in the cords of twins than in the cords of singletons. This difference was not correlated with differences between the two series in respect to gestational age, weight of fetus, or length of cord.

In the twin series, good intrapair correlation in respect to quantitative development of twist was present in sinistral-sinistral cord pairs, irrespective of whether the placentas were monochorionic or dichorionic. There was absence of such intrapair correlation in sinistral-dextral cord pairs.

Support is given to the theory of Schauta that pathological torsion or "twist amputation" of the umbilical cord is a sequel, not a cause, of death of the fetus.

It is proposed that the twist of the normal umbilical cord (as well as the twist of the cord subsequent to death of the fetus) is the result of a rotatory movement imparted to the embryo by the asymmetrical contraction of the uterus.

It is proposed that the direction of the twist is determined by the position of the embryo in relation to the effective axis of torsion of the uterus. The defective quantitative development of twist in one member of a sinistral-dextral pair of twin cords is referred to putative factors tending to maintain "normal" intrauterine orientation of an embryo, despite the deviations of direction inherent in multiple pregnancy.

A mechanical model is demonstrated, as an aid in the understanding of the mechanism of production of the types of twist observed in cords.

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THE USE OF RADIUM IN THE TREATMENT OF BENIGN LESIONS OF THE UTERUS: A CRITICAL TWENTY-YEAR SURVEY*†

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PRIOR to 1940, patients at or about the menopause who suffered abnormal uterine bleeding—the result of dysfunctional uterine bleeding or minimal myomas—were usually treated with radium or x-radiation. In recent years, more and more of these women have been subjected to hysterectomy. This change in the definitive treatment of such lesions was stated to be justified for the following reasons:

1. Some irradiated patients would have recurrent bleeding.
2. A small adnexal lesion (granulosa- or theca-cell tumor of the ovary or adenocarcinoma of the tube) might be overlooked.
3. A small endometrial polyp or early adenocarcinoma of the endometrium might be missed at curettage.
4. Sarcoma might develop later.
5. The uterus might become the site of endometrial or cervical carcinoma in later years.

In 1946, Corscaden[1] presented statistical evidence which led him to conclude that patients with benign uterine lesions treated by radiotherapeutic castration might show an excessive incidence of subsequent uterine carcinoma. He urged the discontinuation of radiation therapy and the serious consideration of prophylactic hysterectomy in the treatment of dysfunctional uterine bleeding in perimenopausal women. Other authors[2, 3, 4, 5, 6] arrived at similar conclusions. The inference was drawn by some that radium and x-radiation might act upon the uterus as carcinogenic agents.

At about the same time it was demonstrated,[7] that because of improved preoperative and postoperative care and the liberal use of blood transfusions and antibiotics, hysterectomy was a relatively safe procedure. As a result of these two observations hysterectomy became, in many clinics, the treatment of choice in patients with benign uterine lesions at or about the menopause.

That this change occurred in our institution is suggested by the data presented in Fig. 1. The number of surgical procedures, exclusive of hysterectomy, bears a fairly constant relationship to the total number of patients operated upon from 1934 until about 1944 or 1945. Since 1946, curiously

*This investigation was supported by the Philadelphia Division of the American Cancer Society. We wish to express our appreciation for their support of this study.

†Read before the Obstetrical Society of Philadelphia, April 2, 1953.

enough the year of publication of Dr. Corscaden's[1] paper, the incidence of hysterectomy has increased and the frequency of the use of radium has declined, regardless of fluctuations in the total number of operations performed. However, as the chart illustrates, a few of us continue to use radium. This persistence resulted from our clinical impression that the results of such treatment had been successful and the incidence of subsequent carcinoma low. In addition, we did not believe that the adoption of hysterectomy and the elimination of radium therapy were warranted in view of the purely inferential nature of the evidence which had been presented concerning the carcinogenic action of radiation.

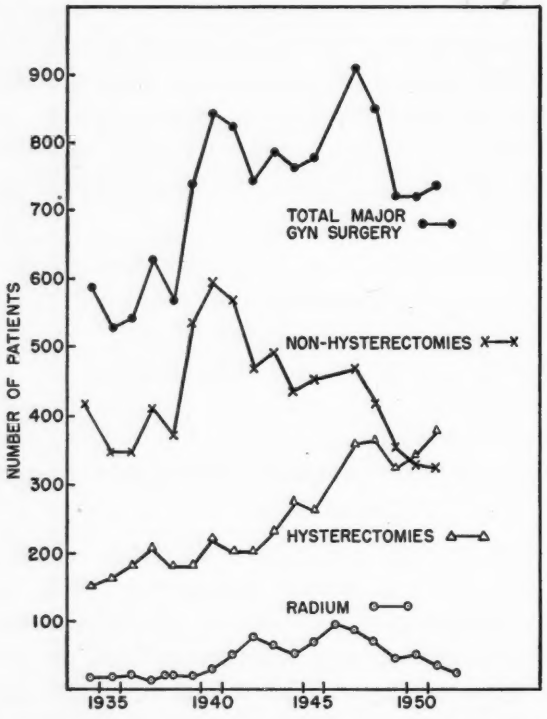

Fig. 1.—Trend in gynecological surgery, Hahnemann Medical College and Hospital, 1934-1952.

Furthermore, when we determined our death rate following hysterectomy for benign lesions of the uterus, we found that in the four-year period, from 1948 to 1951, eight deaths occurred following hysterectomy for benign lesions of the uterus, an uncorrected mortality rate of 0.56 per cent. Study of the clinical history and the pathology of the specimens removed at operation revealed that four of these women were suitable candidates for radium therapy. These four deaths in a four-year period exceed the total number of ovarian and uterine carcinomas that occurred subsequent to radiation therapy in the past twenty years in our institution.

Because hysterectomy was attended by morbidity and mortality in our hands, and because it was our clinical impression that radiation therapy was effective and not followed by a high incidence of postirradiation malignancy,

we continued to use radium therapy. However, in the face of published reports containing contrary opinions, we felt it mandatory to analyze our results. Therefore, we reviewed the records of all patients with benign uterine lesions treated with radium at Hahnemann Hospital from Jan. 1, 1932, to Dec. 31, 1950.

In the summer of 1952, a follow-up study, consisting of contact of patients by letter, telephone, or personal interview, was undertaken. In the majority of cases, a recent pelvic examination had *not* been performed. The patients were classified as "alive and well" if no pelvic complaints, vaginal bleeding or discharge were elicited.

Follow-Up Results in Radiated Patients

Of 765 radium-treated patients, 644 were followed to hysterectomy or to death, or if alive, to 1952 (Table I). With the exception of the years 1933, 1934, and 1935, the yearly follow-up always exceeded 78 per cent and averaged 84.2 per cent for the entire series. Two hundred forty-one patients were treated prior to Jan. 1, 1943, of whom 183 (75.9 per cent) were followed for ten or more years for an average of 13.8 years of follow-up per patient.

TABLE I. DURATION OF FOLLOW-UP

YEARS OF FOLLOW-UP	NUMBER OF PATIENTS FOLLOWED	PERCENTAGE
10-20	183	75.9
5-9	293	86.2
2-4	168	91.3
Total, 2-20	644	84.2

Age.—

Approximately 80 per cent of all the patients followed were 35 to 54 years of age at the time of treatment (Table II). Ninety-nine patients (15.4 per cent) were over 54 years of age and presumably postmenopausal. We are cognizant of the fact that the study of a group of older, postmenopausal women bears no specific relationship to the analysis of results obtained with radium therapy in benign lesions of the uterus in perimenopausal women. Observations of these

TABLE II. AGE AT TIME OF RADIUM THERAPY (FOLLOWED CASES ONLY)

YEARS OF FOLLOW-UP	NUMBER OF PATIENTS FOLLOWED	UNDER 35 YEARS	35-54 YEARS	OVER 54 YEARS	AGE UNKNOWN
10-20	183	5 (2.7%)	145 (79.3%)	22 (12%)	11 (6%)
5-9	293	8 (2.7%)	239 (81.6%)	45 (15.4%)	1 (0.3%)
2-4	168	1 (0.6%)	135 (80.4%)	32 (19.1%)	0
Total	644	14 (2.2%)	519 (80.7%)	99 (15.4%)	12 (1.9%)

patients does provide, however, additional opportunity to study the possible carcinogenic activity of the radium and the effectiveness of the clinical and laboratory procedures which precede treatment.

Clinical Diagnoses.—

The classification of the clinical diagnoses in patients with vaginal bleeding of nonmalignant origin is often difficult because of changing nomenclature and incomplete knowledge of the causes of such vaginal bleeding. For example, the term "postmenopausal uterine bleeding" was used as a diagnosis in patients over 54 years of age in whom no pathologic process was apparent by clinical or laboratory examination. We have classified these cases as "diagnosis unknown." Furthermore, final discharge diagnoses based on only the most obvious findings were entered in the hospital record while less well-defined, but more clinically significant, entities were ignored. As a result, some patients were classified as having cases of chronic cervicitis or cervical polyp, whereas perusal of the charts of these patients, particularly with reference to the history and therapy, suggests strongly that many of them had dysfunctional uterine bleeding in addition to their more evident lesions. Nonetheless, the diagnosis as recorded in the original chart was used as a basis for these statistics.

Patients with the diagnoses of dysfunctional uterine bleeding and/or uterine myomas form the bulk of the women under consideration (Table III). Of the 145 patients aged 35 to 54 years, who were followed for ten or more years, either or both of these two diagnoses were obtained in 122 patients (84.2 per cent). For the whole group of 519 patients (aged 35 to 54 years) more than 80 per cent definitely suffered from one or both of these conditions.

TABLE III. DIAGNOSIS IN RADIUM-TREATED CASES. FOLLOWED CASES ONLY

YEARS OF FOLLOW-UP	NUMBER OF PATIENTS FOLLOWED	DYSFUNCTIONAL UTERINE BLEEDING AND/OR MYOMA	OTHERS AND UNKNOWN
10-20	183	136 (74%)	47 (26%)
5-9	293	193 (66%)	100 (34%)
2-4	168	105 (63%)	63 (37%)
Total	644		

TABLE IV. SUMMARY OF RESULTS

AGE (YEARS)	YEARS OF FOLLOW-UP	NUMBER OF PATIENTS	TREATMENT FAILURES		POSTIRRADIATION MALIGNANCY		POSTTREATMENT MORBIDITY	
			NO.	%	NO.	%	NO.	%
54 and under	10-20	150	16	(10.7)	3	(2.0)	1	(0.7)
	5-9	247	6	(2.4)	0	(0.0)	1	(0.4)
	2-4	136	0	(0.0)	0	(0.0)	0	(0.0)
	2-20	533	22	(4.1)	3	(0.6)	2	(0.4)
55 or more	2-20	99	3	(3.3)	0	(0.0)	0	(0.0)
Unknown	2-20	12	0	(0.0)	0	(0.0)	0	(0.0)
All ages	2-20	644	25	(3.9)	3	(0.5)	2	(0.3)

Mortality, zero.

Radium Dosage.—

There has been a progressive increase in the radium dose utilized in this series (Fig. 2). The heavy dotted line signifies 1,800 mg. hr. In the period from 1932 to 1942 few patients received as much as this dose, whereas the vast majority of women treated in 1948-1950 received more than 2,000 mg. hr.

The effectiveness of radium therapy in benign lesions of the uterus is difficult to evaluate. The diagnostic and therapeutic procedures which precede radium therapy doubtless aided in curing many of these women of their vaginal bleeding. Unfortunately, we have no significant perimenopausal group of patients with vaginal bleeding of benign origin treated by dilatation and curettage alone and followed for ten or more years. Therefore the value of radium therapy in our patients cannot be determined by comparison with such a control group. We can, however, evaluate the treatment in terms of the therapeutic failures and postirradiation morbidity and malignancy.

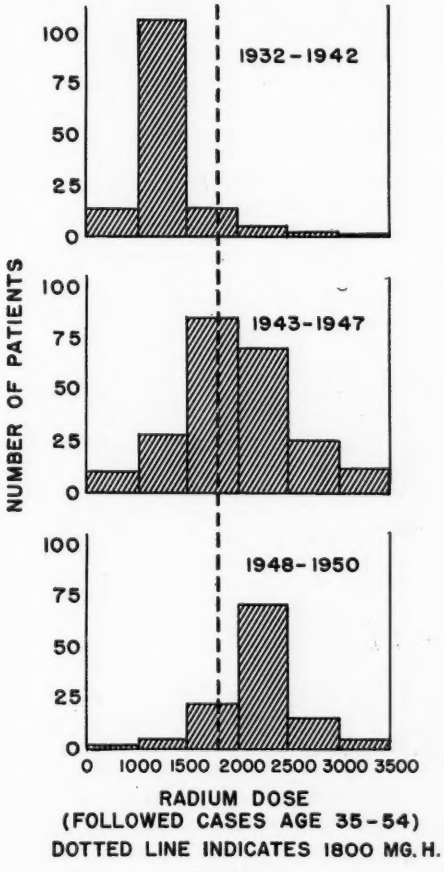

Fig. 2.

Treatment Failures.—

Of the 644 patients followed 28 were hospitalized for further gynecologic treatment at some time following their initial radium therapy (Table IV). Twenty-three women had recurrent dysfunctional uterine bleeding and two

suffered uterine prolapse, resulting in an incidence of 3.9 per cent treatment failures of benign origin, occurring three months to sixteen years post radiation. Three patients developed pelvic malignancy, an incidence of 0.5 per cent.

Postradiation Complications.—

There were only two significant postradiation complications. One patient developed a pelvic abscess which required colpotomy. Another patient suffered pelvic cellulitis which subsided with medical treatment. No deaths attributable to radium therapy occurred.

Postradiation Pelvic Malignancy.—

The three carcinomas appeared six, twelve, and fourteen years following radiation (Table V).

TABLE V. POSTRADIATION MALIGNANCY CASES (3)

	ELAPSED YEARS BETWEEN RADIUM TREATMENT AND DIAGNOSIS OF MALIGNANCY	ELAPSED YEARS SINCE TREATMENT OF CANCER
Adenocarcinoma No. 1	6	6
Adenocarcinoma No. 2	12	8
Pseudomucinous cystadenocarcinoma of ovary	14	4

CASE 1.—A 30-year-old patient was treated for dysfunctional uterine bleeding in 1940 by dilatation and curettage and 1,200 mg. hr. of radium. In 1946, at 36 years of age, the patient was treated by hysterectomy because of vaginal spotting. No preliminary curettage was performed. Tissue removed revealed extensive endometrial carcinoma with tubal involvement and small uterine myomas. The patient is alive and free from pelvic malignancy six years postoperatively. Review of the slides of the original curettings corroborated the initial pathological diagnosis of endometrial hyperplasia.

CASE 2.—A 54-year-old patient with postmenopausal bleeding of unknown origin was treated by dilatation and curettage and 1,200 mg. hr. of radium in 1932. In 1944, at 66 years of age, the patient was again curetted because of a profuse, watery, nonsanguineous vaginal discharge. Biopsy revealed endometrial adenoacanthoma. Three thousand nine hundred mg. hr. of radium was administered, and total hysterectomy and bilateral salpingo-oophorectomy were performed. Persistent malignancy was demonstrated in the removed uterus. The patient is alive and free from pelvic malignancy eight years postoperatively. Review of the slides of the original curettings confirmed the initial diagnosis of endometrial hyperplasia.

CASE 3.—A 44-year-old patient was treated by dilatation and curettage and 1,200 mg. hr. of radium in 1934 because of intermenstrual spotting. In 1948, at 58 years of age, a salpingo-oophorectomy was performed for an apparently benign cystic tumor of the ovary. Areas of malignancy were demonstrated within the tumor on microscopic examination. The patient is alive and free of any evidence of malignancy four years postoperatively.

Comment

The effectiveness of radium therapy in the treatment of benign lesions of the uterus in our patients seems apparent. As the "routine" dose was increased, the incidence of treatment failures decreased. Since 1947, over 75 per cent of our patients treated each year received more than 2,000 mg. hr.

There have been no failures since this dosage schedule has been employed. This success is the result of the increased radium dose and is not significantly related to the brevity of the follow-up of the cases treated in 1948, 1949, and 1950. This conclusion is warranted by the fact that 32 per cent of the patients who required retreatment had the second episode of bleeding within two years of the initial radiation. It is, therefore, reasonable to assume that the eventual failure rate will be low in the group treated during 1948 to 1950 for there has been no treatment failure among them to date.

As stated previously, the success in treatment of women with benign uterine lesions at or about the menopause is the result, in part, of the diagnostic and therapeutic procedures which accompany the radium application. Whatever the reason, over 95 per cent of our patients have been successfully managed by the use of these procedures and radium. We know of no similar group of patients treated by dilatation and curettage, with or without polypectomy and/or cervical conization that has achieved this degree of relief. It may be that our success in the treatment of postmenopausal women, regardless of indication, and premenopausal women with diagnoses other than dysfunctional uterine bleeding or myoma may bear no relationship to the use of radium at all. Nonetheless, analysis of the data from our patients, aged 35 to 54, with the diagnoses of dysfunctional uterine bleeding and myoma only, demonstrates that over 93 per cent were treated successfully. This result is significantly better than the usually quoted cure rate of 40 to 60 per cent with curettage alone.

This investigation does not permit any conclusions concerning the specific problem of *when* radium therapy shall be used for the treatment of dysfunctional uterine bleeding or minimal myomas in perimenopausal women. However, our data *do permit* observation of the effectiveness of radium therapy in such uterine bleeding, and the results indicate that radium can be used successfully in such women with minimal morbidity and no mortality. For these reasons, we believe that when definitive therapy is required for dysfunctional uterine bleeding or minimal myomas in women at or about the menopause, radium is the treatment of choice because it is a safe and effective therapeutic agent.

The progressive decrease in the use of radium for such benign lesions of the uterus of perimenopausal women since 1946 has not stemmed from the belief that radium is an ineffective method of therapy, but from fear of subsequent uterine carcinoma. The initial impetus to the development of this anxiety was provided by Corscaden[1] who reported 15 cases of uterine carcinoma (6 cervical and 9 endometrial) in 958 patients with uterine bleeding who had been treated by radiation castration. He concluded on the basis of statistical analysis of the data that the eventual number of malignancies in his patients (9.6 per cent) would be 3.4 times as large as the number of cases of uterine carcinoma anticipated in the general population, quoted to be 2.8 per cent.[8] This anticipated high incidence of carcinoma in the radiated patients was obtained by comparison of the rate of change in the death rate of women in the general population during aging to the rate of change in the incidence of carcinoma in his irradiation-treated population as they grew older. We question the validity

of the conclusion that the incidence of carcinoma of the uterus will be significantly higher in the radiation-treated patients for two reasons. First, it must be recognized that the incidence of carcinoma of the uterus in the general population is unknown for each year of life and that Dr. Corscaden assumed that the death rate and the uterine carcinoma rate bear a reasonably fixed relationship to each other at any age over 30. The truth of his thesis rests largely upon this assumption. Second, the incidence of carcinoma of the uterus following irradiation in his report represents one of the highest ever reported.

In addition, his report indicated that the ratio of patients with adenocarcinoma of the endometrium to carcinoma of the cervix is high in women who were previously irradiated for benign lesions. These data were advanced as evidence for the thesis that patients with abnormal uterine bleeding have a greater tendency to develop endometrial adenocarcinoma. This concept is not new. Taylor,[9] Novak and Yui,[10] and Randall[11] have called our attention to the frequent association of cases of abnormal bleeding at or about the menopause revealing endometrial hyperplasia, and the development of endometrial carcinoma postmenopausally. Despite this, Dr. Corscaden's[1] paper, "Carcinoma Subsequent to the Radiotherapeutic Menopause," is commonly misinterpreted to suggest some carcinogenic activity of radium. This is in complete disagreement with the text and the conclusion of his paper and we quote: "It is inferred that the endometria which bleed abnormally prior to the menopause are predisposed to the subsequent development of carcinoma of the corpus." Nowhere in his paper, other than in the title, is it even inferred that radium is carcinogenic.

Another approach to the problem of the incidence of postradiation malignancy was that of Speert and Peightal.[5] These authors reported on 270 cases of uterine malignancy of which 21 had been previously radiated. This 8 per cent incidence of prior radiation among the patients with malignancy suggested to them that radium was carcinogenic in its action. It is interesting to note that 32 per cent of their patients with postradiation malignancy had sarcoma of the uterus. Corscaden[1] found no cases of sarcoma in 958 cases followed; Smith and Bowden[3] none in 946 cases; Hundley, Diehl, and Kardash[12] none in 175 cases; Montgomery, Long, and Hoffman[13] none in 851 cases; and ourselves, none in 644 cases. This, again, demonstrates that there is little uniformity in small samples and for this reason conclusions drawn from such data can hardly be taken as fact at this time.

Another objection to radium therapy, previously noted, is that vaginal examination may occasionally miss an early adenocarcinoma of the tube or a small functional tumor of the ovary. We do not believe that such fears warrant the discontinuation of radium therapy for in our own group of 644 cases only two adnexal lesions occurred and these appeared fourteen and sixteen years after radiation therapy. However, because of concern with these possibilities, radium should never be utilized in the presence of even questionable adnexal disease.

As previously stated, this survey does not permit any conclusions concerning the specific problem of when radium should be used in the treatment of dysfunctional uterine bleeding or minimal uterine myomas. We are opposed to the indiscriminate use of radium therapy. The following represent our concept of poor candidates for radiotherapeutic castration:

1. Young women in whom ovarian function should be preserved.
2. Perimenopausal women who have an unfounded fear of radium therapy.
3. Emotionally unstable menopausal women who attach undue importance to the preservation of their ovarian function.

It is our belief, however, that the use of hysterectomy as the *sole* definitive therapy for benign lesions of the uterus at or about the menopause will not produce any net saving of years of life. A few malignancies will be prevented, but routine treatment by hysterectomy will not only lose an occasional life, but also lose it at a considerably earlier age. In addition, if we compare the incidence and severity of the complications produced by these two forms of treatment, the economic cost of these procedures in terms of hospital and physicians' fees, plus wages lost because of length of convalescence, it is obvious that radium therapy is safer and less expensive.

In closing, as a result of our experience with this survey, we urge a more conservative and rational approach to the definitive treatment of benign lesions of the uterus in women at or about the menopause. The trend to hysterectomy is primarily based upon a concern over an alleged high incidence of postradiation malignancy. This has never been demonstrated by the analysis of actual clinical experience[12, 13] but only inferred by statistical prognostication. Therefore, it does not seem reasonable to us to expose our patients to hysterectomy when there is available an effective and inexpensive treatment whose immediate and remote safety has been demonstrated.

We wish to thank the members of the Division of Women, Hahnemann Hospital, Philadelphia, for their cooperation in the follow-up study of the private patients included in this survey, and Dr. Newlin F. Paxson, Chief of the Division of Women, for his advice and criticism of the typescript.

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PHYSIOLOGICAL SALPINGITIS

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IN THE course of routine examination of Fallopian tubes removed at the time of hysterectomy in the Free Hospital for Women, numerous cases of acute salpingitis associated with menstrual endometrium have been encountered. While the inflammatory reaction was of the acute variety and was associated with an infiltration of polymorphonuclear leukocytes, it did not have the precise pathologic appearance of acute salpingitis due to bacterial infection. Because many of these tubes contained menstrual debris in their lumina and because the inflammation seemed to be present only at the time of menstruation, it seemed reasonable that regurgitation of menstrual blood into the lumina of the tubes was responsible for this inflammatory reaction.

It is the purpose of this report to describe the histologic picture of this salpingitis and discuss its possible cause.

Materials and Methods

All Fallopian tubes were selected which were removed surgically during the past two years in cases where the associated uterus showed menstruating endometrium. The microscopic sections of the tubes and the endometrium were reviewed. The cases with obvious salpingo-oophoritis due to bacterial infection of short or long duration were excluded from the series. The histories of patients with acute salpingitis, apparently related only to the menstrual phase of the cycle, were then reviewed with special attention to the patient's age, obstetrical history, dysmenorrhea, and premenstrual tension.

The endometrium was evaluated from the standpoint of whether it was early, mid-, or late menstrual endometrium and the cases were segregated on this basis. This was done in order to determine whether the apparent intensity of the inflammation varied during the menstrual period.

In order to determine whether or not the inflammation was due to bacterial infection, MacCallum-Goodpasture stains were done on all the cases in this group.

Observations

Of 69 patients who had hysterectomy and salpingectomy at the time of menstruation 43, or 62.3 per cent, showed some degree of inflammation of the tubes. The inflammatory reaction was largely characterized by polymorphonuclear leukocytes within the lumen of the tube, in the stroma of the tubal plicae, but only rarely in the inner portion of the muscular wall (Fig. 1). Also the plicae showed edema (Fig. 2), stasis of leukocytes within their capillaries (Fig. 3), and dilatation of their lymphatics (Fig. 4). The inflammation was for the most part confined to the mucosal region of the tube, and the muscular

walls were very seldom involved. When such involvement was present, it was the inner portion, nearest the lumen of the tube, that showed the inflammatory reaction.

Signs of chronic inflammation in the plicae of these tubes were not found. The mucosa showed no evidence of healed follicular salpingitis, infiltration of lymphocytes or plasma cells or fusion of the tips of the plicae. In about half

Fig. 1.

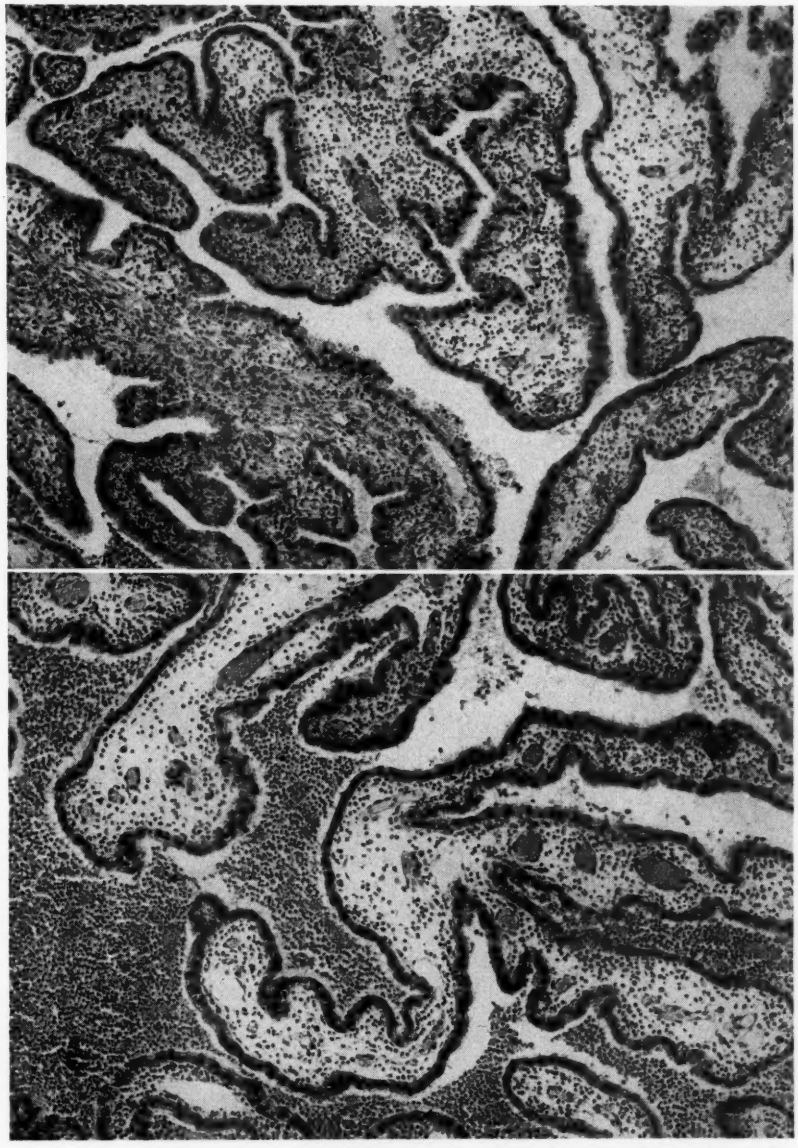

Fig. 2.

Fig. 1.—Inflammation of plicae with polymorphonuclear leukocytes in stroma and lumen of Fallopian tube. The endometrium in this case was in the early stage of menstruation. (FHW, S-51-4057.) (Hematoxylin and eosin. ×170. Reduced one-third.)

Fig. 2.—Edema of plicae, leukocytic infiltration of stroma, red blood cell and endometrial debris in lumen, numerous polymorphonuclear leukocytes in lumen of Fallopian tube. Same tube as Fig. 1. (FHW, S-51-4057.) (Hematoxylin and eosin. ×170. Reduced one-third.)

the cases, however, a perivascular cuff of lymphocytes around small vessels in the muscularis was seen. Usually only one or two such accumulations were found in any one tube.

In Fig. 5 the cases with "physiological salpingitis" have been arranged according to the time of removal of the uterus relative to the stage of menstruation. Early menstruation corresponds to the first day of bleeding; mid-menstruation to the second and third days, and late menstruation to the

Fig. 3.

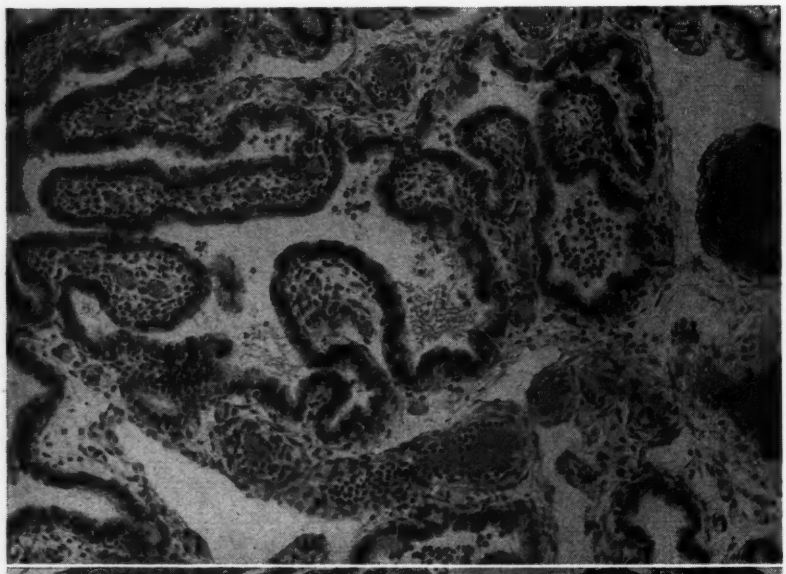

Fig. 4.

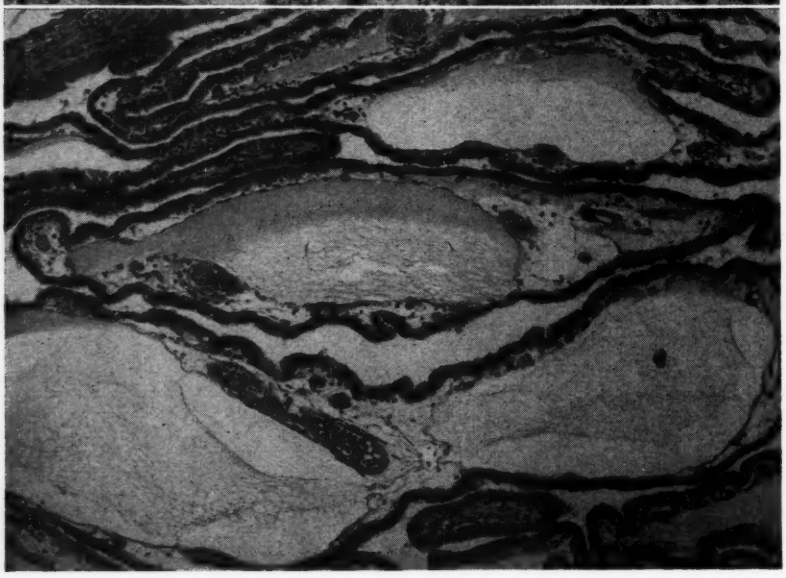

Fig. 3.—Stasis of leukocytes in small vessels in the plical folds of the Fallopian tube. The endometrium was in the mid-stage of menstruation. (FHW, 5-52-3861.) (Hematoxylin and eosin. ×240. Reduced one-third.)

Fig. 4.—Dilatation of lymphatic vessels in plicae of Fallopian tube. The endometrium of this case was in the mid-stage of the menstrual period. (FHW, 5-52-2703.) (Hematoxylin and eosin. ×170. Reduced one-third.)

fourth and fifth days. In each column are placed the number of cases exhibiting various aspects of these active inflammatory changes, regardless of the severity of the reaction.

It is apparent that the majority of the cases occurred in the mid-menstrual period. The table also indicates that the proportion of tubes involved by each type of pathologic change was greater in the mid-menstrual period than in the

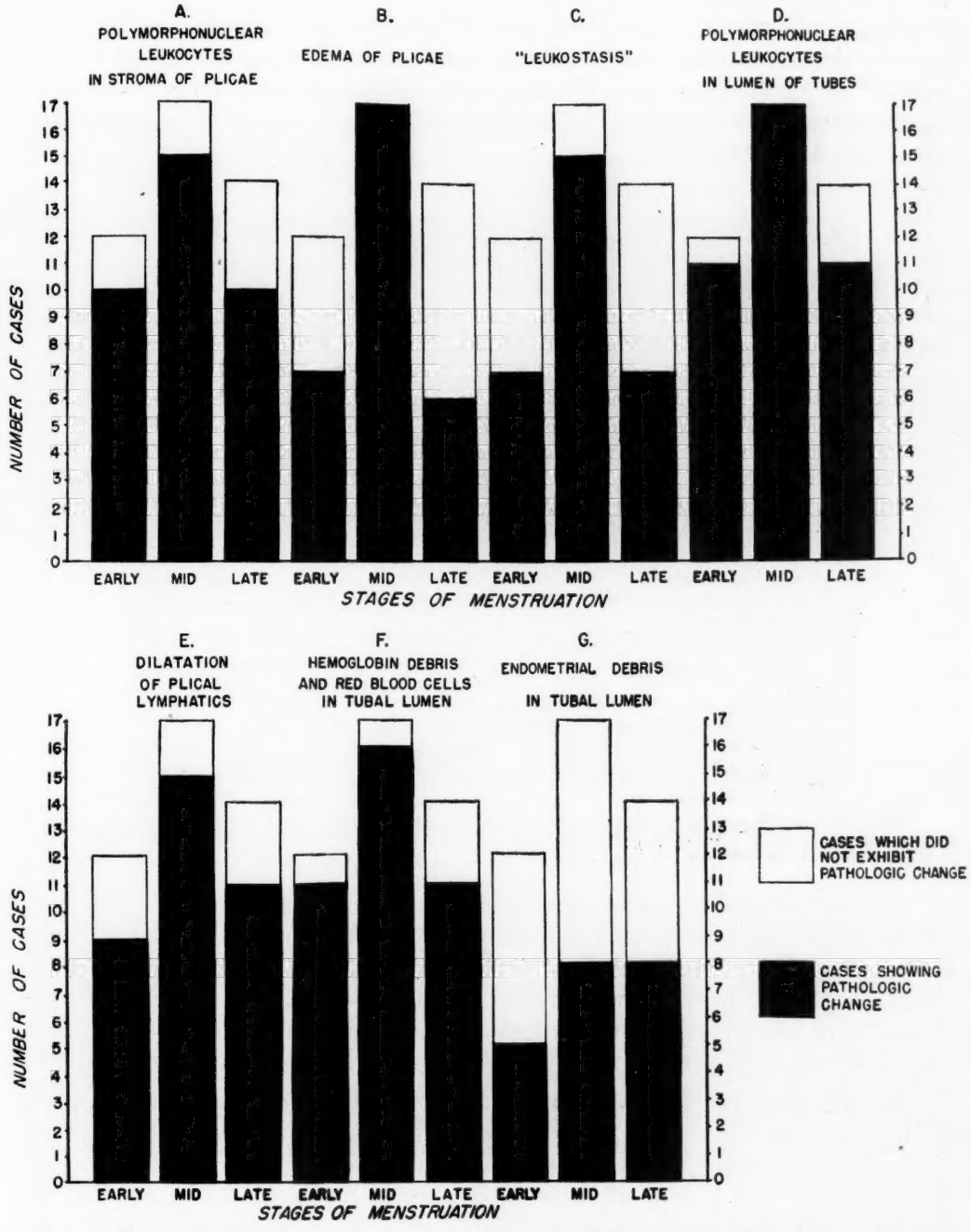

Fig. 5.—The number of cases showing the different morphologic changes associated with acute physiological salpingitis during the menstrual period.

early or late stages. This means that in the mid-menstrual stage the tubes were more likely to exhibit most of these changes whereas in the early or late stages only one or two of the changes might be found. Although it is not presented in the chart, it was also noted that all of these reactions were in general much more intense in the mid-menstrual stage. From the observations presented in Fig. 5, *A*, it appears that infiltration of the plical stroma with polymorphonuclear leukocytes is found shortly after the onset of menstruation, becomes more pronounced at the height of menstruation, and persists, although in lesser degree, into the phase of late menstruation. This same rise and decline was found for edema of the plical stroma, *B*, leukostasis, *C*, the presence of polymorphonuclear leukocytes in the lumen of the tube, *D*, and dilatation of the plical lymphatic vessels, *E*.

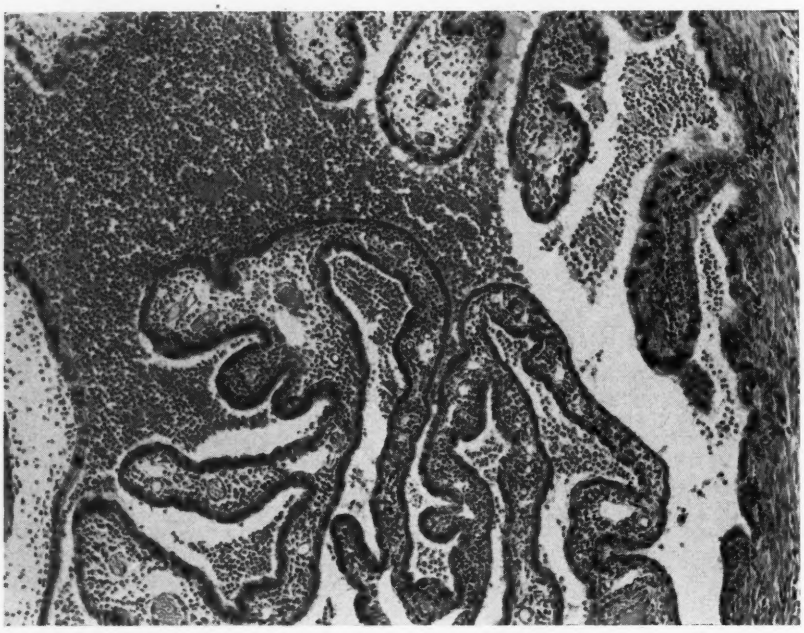

Fig. 6.—Red blood cells, hemoglobin and endometrial debris in lumen of Fallopian tube, associated with early menstrual endometrium. (FHW, 5-51-4057.) (Hematoxylin and eosin. ×170. Reduced one-third.)

Polymorphonuclear leukocytes were noted in the lumina in all but 4 of the 43 cases. Red blood cells and hemoglobin debris were also found in the tubal lumen from the onset of menstruation (Fig. 6). However, identifiable fragments of endometrium were found in only about half the cases. Macrophages were also present in the lumina of the tubes in about half of the cases and appeared to be present more often in the late stages of menstruation.

In only 8 of the 43 cases was there any evidence of acute inflammation of the muscular wall. This was manifested by a slight leukocytic infiltration of the inner muscular layers nearest the tubal lumen and was never seen deep in the muscle wall. None of these tubes showed any evidence of necrosis or change of any kind in the tubal epithelium, nor was there any necrosis of con-

nective or muscle tissue. MacCallum-Goodpasture stains failed to reveal any bacteria in the tubal lumen, the plical connective tissue, or the muscular walls of any of these tubes. All of these patients had elective operations and none of them exhibited clinical evidence of infection prior to operation. One or two vessels of the muscular wall of over half of these tubes were surrounded by a small collection of lymphocytes. Since the acute reaction never involved the muscle at the depth of these vessels, the relationship of the lymphocyte collection to "physiological salpingitis" seems remote.

Of the 43 cases, both tubes were available for study in 28 cases, whereas only one tube was present in 15 cases. In 5 of the cases where both tubes could be studied, the inflammatory reaction was unilateral. In a control group of several hundred cases, this inflammatory reaction was not found in the tubes associated with proliferative or secretory endometrium of the remaining 23 days of the endometrial cycle. The oldest patient with physiological salpingitis was 54 years and the youngest was 25 years, while the average age of these patients was 40 years. Of these 43 patients, 9, or 20.9 per cent, had never been pregnant while the average parity of the remaining 34 patients was 2.4. Dysmenorrhea unassociated with endometriosis was present at the time of surgery in 10, or 23.2 per cent, of these patients. In 7 of these 10 patients there was a previous history of dysmenorrhea with the onset ranging from several months to many years prior to surgery. The remaining 3 patients had a history of dysmenorrhea which was present for the first time at the time of surgery. One of the patients gave a history of previous dysmenorrhea but did not complain of this symptom at the time of surgery. A history of premenstrual tension was obtained in only 3 of the 43 cases, or 6.9 per cent.

Uterine leiomyomas were found in 19 of the 43 cases. In addition, 7 of these 19 had associated endometriosis and there were 5 cases in which the primary pathology was endometriosis. There was one case of carcinoma in situ of the cervix and two cases of invasive carcinoma of the cervix and one case of cancer of the breast. It is interesting to note that in only one of these 43 cases was free blood found in the peritoneal cavity. In this particular case the blood was described as dark red, fluid, about 20 c.c. in amount, and the source of this blood was not noted by the surgeon.

Comment

The inflammation of the Fallopian tubes described in this report is unique. Because no bacteria were demonstrated and because the patients presented no evidence of infection clinically, it is considered unlikely that it is bacterial in origin. On the other hand, the inflammation occurred only during the menstrual period and not at other times in the menstrual cycle. Endometrial debris as well as polymorphonuclear leukocytes and red-cell debris were found in the tubal lumina, and, because the inflammation was superficial and submucosal, it is suggested that the cause is related to the regurgitation of menstrual blood into the tubes during the menstrual period. Another piece of evidence that adds support to this concept is found in an experiment of

Dr. G. V. Smith who injected human menstrual blood into one horn of a rabbit uterus and left the other horn untouched as a control. The injected side became purplish red and swollen, while the control side exhibited no change. Microscopically, the injected horn revealed an intense mucosal and submucosal inflammation which was characterized by an infiltration of polymorphonuclear leukocytes in the submucosal connective tissue, and leukostasis (Fig. 7). This histologic picture is practically identical with that seen in these human Fallopian tubes at the time of menstruation.

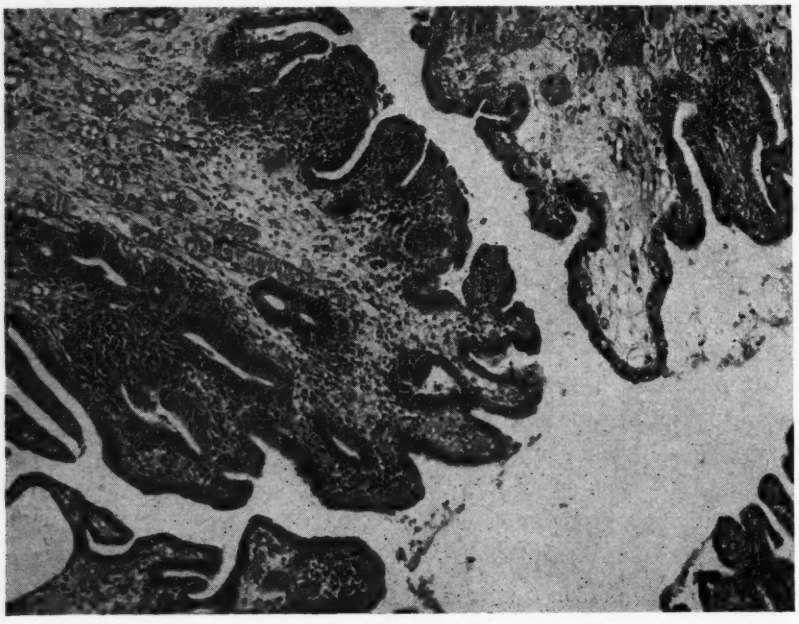

Fig. 7.—Horn of rabbit uterus injected with human menstrual blood showing mucosal and submucosal inflammation. (Experimental material from Dr. G. V. Smith.) (Hematoxylin and eosin. ×200. Reduced one-third.)

The inflammation, while occasionally severe, does not appear to leave any residual damage to the tube. Even during the acute phase there is no evidence of necrosis or destruction of any of the tubal structures. Other interesting features of this reaction are its short duration, lasting only as long as menstruation and the fact that there is no residual chronic reaction detectable histologically. These findings suggest an etiological agent that produces the reaction only as long as it is present, and which allows prompt and complete recovery.

The nature of the toxic material in menstrual blood has been extensively studied by the Smiths.[2] They have demonstrated that menstrual blood contains a substance which is lethal to immature rats. The local reaction in these animals is characterized by massive edema and a moderate polymorphonuclear leukocytic infiltration. The toxic material is concentrated in the endometrial debris, is extremely labile, and is associated with a proteolytic enzyme. It is suggested that this is the substance responsible for "physiological salpingitis." It is interesting to note that lochia also contains a substance which is lethal to rats and which produces intense local edema.

Hellman[1] has recently described an acute salpingitis which appears to be histologically identical with that described in this report. The 715 pairs of tubes in his study were obtained at the time of sterilization on various days of the puerperium. He found an acute salpingitis of mild to moderate degree in one out of three cases in the sixth to eighth days of the puerperium. It was rarely found in the first four days. Since bacteria were not found in these tubes, Hellman referred to the inflammation as one of nonspecific origin.

It seems likely that the inflammation following pregnancy described by Hellman is similar to that occurring in the tube at the time of menstruation. It is possible that the decidua which is in the process of involution and necrosis after delivery might be regurgitated into the tubes in a manner similar to the regurgitation of menstrual blood.

Since not every patient at the time of menstruation has this type of inflammation, it may be that not every patient regurgitates menstrual blood into the tubal lumen. Therefore mechanical factors are probably important in conditioning the appearance of the inflammation. It is possible that this phenomenon may occur often or only occasionally in any one individual.

The question as to whether or not this inflammation produces any clinical symptoms is of some interest. It has been demonstrated by Theobald[3, 4] that the Fallopian tubes are the most sensitive of all the pelvic organs to pain stimuli. In the small series presented in this report, about one-fourth of the patients complained of dysmenorrhea at the time of the operation and a few of these had dysmenorrhea during previous menses. Of the 26 patients who were menstruating but who had negative tubes, only 4 (15 per cent) had dysmenorrhea. From these observations it seems possible that the pain in certain cases of dysmenorrhea may be initiated by this transient acute "physiological salpingitis."

Summary

A nonbacterial acute salpingitis occurring at the time of menstruation was found in 62.3 per cent of patients who were menstruating.

The inflammatory reaction was characterized by a polymorphonuclear leukocyte infiltration, edema of the stroma of the plicae, dilatation of lymphatic vessels of the plicae, leukostasis, and menstrual blood in the tubal lumen.

The possible origin and significance of this inflammatory reaction have been discussed.

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COMPARATIVE BACTERIOLOGY OF VAGINAL TRICHOMONAD INFESTATIONS*

A Study of 190 Clinical Cases

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CHANGES occurring in the microbial flora of the human vagina infested with the flagellate, *Trichomonas vaginalis,* have been the cause of controversy since this protozoan parasite was first described by Donné in 1836.[5] The number of zoologists contributing to the study of the parasitology of the disease syndrome known as trichomonad vaginitis and the documented evidence of innumerable physicians with a multitude of remedies for its cure are eminently presented by Trussell[18] in his monograph of 1947. Researches directed toward a correlation of the pathology of the urogenital tract and associated microorganisms have been numerous as indicated by the voluminous literature on the subject. Review of the literature fails, however, to reveal precise data which present the bacterial flora associated with trichomonads in the human female genitourinary tract as compared to the so-called normal vaginal organisms, following isolation by exacting pure-culture techniques.

Hite and associates[9] isolated a variety of bacteria from the postpartum uterine cavities of normal patients and those with endometritis and from the vaginas of trichomonad-infested patients. Both groups presented a similar flora. Studies by Kessel and Gafford[11] indicated that *T. vaginalis* was associated with cases of trichomonad vaginitis but that no one bacterium or fungus isolated was more common in persons with such symptoms of vaginitis than in normal individuals. The only organisms found with any degree of consistency in patients with a trichomonad vaginitis by Stein and Cope[17] were the Döderlein bacilli and gram-positive nonhemolytic streptococci. Identified streptococci were classified as *S. ignavus, S. salivarius* and *S. hemolyticus III.*

Hibbert[7] noted the presence of a short-chain, gram-positive, nonhemolytic streptococcus in active vaginitis unassociated with the flagellate, *T. vaginalis.* Later, Hibbert and Falls[8] isolated and established the pathogenicity of *Streptococcus subacidus* by experimental inoculation of volunteer patients with pure cultures of the organism.

In an evaluation of the microflora associated with trichomonads, Bland and Rakoff[1] found diphtheroid rods common but not more prevalent in women

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with trichomonad vaginitis than in noninfected patients. Small gram-negative cocci were evident in 55 per cent and gram-negative bacilli in 75 per cent of some 267 patients.

Karnaky[10] has shown Döderlein bacilli and various cocci to be present in trichomonad infestations. Curtis[4] encountered at least four types of gram-negative diplococci in a study of chronic leukorrhea, and found gram-positive diplococci almost always present in cases subject to recurrent symptoms of acute inflammation.

Trussell[18] stated that much work remains to be done on the various bacterial species which can be isolated from the human vagina, with a re-evaluation of data in the light of contemporary bacteriological concepts.

The present investigation deals with bacteriological data obtained from a series of 104 patients manifesting clinical symptoms of the syndrome, *Trichomonas vaginalis* vaginitis, and from a series of 86 normal flagellate-free patients. Comparison of the microbial flora in the groups was made in an attempt to show if bacteria or fungi play a significant role in this type of vaginitis.

Material and Methods

The clinical and laboratory criteria employed for the diagnosis of vaginal trichomonad infestations have been presented in an earlier publication.[14]

Patients selected for the present study possessed a characteristic vaginal discharge of a malodorous, frothing, watery nature, from which motile trichomonads could usually be observed in hanging-drop preparations. Vaginal discharges were collected aseptically with an unlubricated speculum and distributed immediately with sterile cotton swabs to one tube each of a group of three media: (1) 10 ml. protein hydrolysate medium[12, 13] for isolation and cultural confirmation of vaginal trichomonads, (2) a 12 ml. deep tube of Linden thioglycollate medium (Difco) for anaerobic bacteria, and (3) 8 ml. of tryptose phosphate broth enriched with 2 per cent ascitic fluid for aerobic bacteria.

The tubes were usually received in the laboratory within three hours after collection of the specimens, and incubated at 37° C. for 16 to 24 hours. Following this primary incubation period, the flagellate medium was centrifuged at 1,200 r.p.m. for 15 minutes and the sediment examined for motile flagellates to confirm a diagnosis of trichomonad vaginitis. The use of this specific flagellate medium[12] aided in the confirmation of eight cases where the original discharge material was called negative from hanging-drop preparations.[14] All flagellate cultures were further confirmed by iron-hematoxylin stained mounts.

From the thioglycollate medium, subcultures were made to trypsin digest and thioglycollate agar plates. Examinations were made at 48 hour intervals, and plates were discarded as negative when no colony formation could be noted after three weeks. When growth was obtained, transfers were made to thioglycollate broth and chopped meat-brain infusion broth tubes. Anaerobic isolates were maintained on 5 per cent blood-dextrose agar in a Novy jar. A detailed study of these organisms is to appear in a subsequent publication.

Subcultures were made from the aerobic broth medium to desoxycholate-citrate agar, 5 per cent blood-dextrose agar, and to duplicate tubes of Sabouraud's dextrose agar. Of the latter medium, one tube was incubated at room temperature and the other at 37° C. Bacteria appearing on desoxycholate-citrate agar or blood agar plates were fished to brain infusion broth for pure culture studies. Sabouraud's medium was examined for yeasts or molds at 72 hour

intervals over a period of one month. Such forms isolated were subcultured for identification.

Bacteria isolated in pure culture were classified by the Bergey schema.[2] Organisms of the coli-aerogenes group were routinely subcultured to tryptophane broth for detecting indol production, to MR-VP medium (Difco) for methyl red and Voges-Proskauer tests, and to Simmons' citrate medium to determine the utilization of citrate salts as a carbon source. Carbohydrates were employed in 0.5 per cent concentration in phenol red broth containing 0.1 per cent agar. Those used routinely included dextrose, lactose, maltose, mannite, sucrose, and xylose, and, when indicated, additional reactions were observed in galactose, glycerol, levulose, raffinose, salicin, and sorbitol. All organisms were cultured in gelatin and purple milk medium.

Chapman's tellurite medium[3] was used to isolate streptococci. These isolates were subcultured in neopeptone broth medium.[15] Growth reactions in brain infusion broth containing 6.5 per cent sodium chloride, Hiss' serum medium, and in brain infusion broth buffered at pH 9.3 were determined. Bile solubility tests were performed routinely. A 5 per cent suspension of washed rabbit erythrocytes was used to ascertain lytic ability. Lancefield group determinations were made on all beta-hemolytic organisms recovered from blood agar plates.

Staphylococci were observed for hemolytic activity, pigment production, catalase production, and further classified by biochemical reactions.

Results and Comment

The organisms constituting the vaginal microflora in 104 patients classified as having a trichomonad vaginitis are presented in Table I. These bacteria may be compared and contrasted with organisms recovered from the vaginal vault of 86 normal patients comprising the control series. A total of 755 organisms were isolated from 190 patients. Some 749 organisms were identified in pure culture and classified in 26 species.

It is noted immediately that the two series are very similar as to species of organisms isolated and relative percentile values. Of particular interest is the fact that those organisms to which a pathogenic nature is attributed such as *Proteus vulgaris, Pseudomonas aeruginosa* and hemolytic streptococci appear not only in trichomonad-infested cases but also in the normal vagina. In some instances, the prevalence is slightly greater in the patients free of the protozoan.

The presence of Döderlein bacilli or diphtheroid rods, the so-called "index" to the healthy vagina, is approximately the same in both series. These data differ from those of Lissimore and Currie[16] who found Döderlein bacilli in only 1 of 71 cases of vaginal trichomoniasis. They reported hemolytic streptococci in 9 per cent, *Staphylococcus aureus* in 30 per cent and *E. coli* in 7 per cent of their cases. In the current investigation, the incidence values of these organisms are 20, 19, and 32 per cent, respectively.

The frequency of common staphylococci and small groups of miscellaneous organisms including species of Gaffkya, Sarcina, Alcaligenes, Aerobacter, and Vibrio appears quite similar in both series. It is believed that no particular significance may be stressed for these groups due to their ubiquity and low-grade or negligible pathogenic nature.

In only three instances were dual infections with *Candida albicans* and *T. vaginalis* noted. Approximately 15 per cent of the normal control patients harbored nonpathogenic yeasts, whereas 22 per cent of the flagellate-infested individuals possessed these organisms.

The results presented here do not support the view of Hibbert and Falls[8] that *Streptococcus subacidus* causes a specific vaginal discharge. In fact a greater number of nonhemolytic streptococci were isolated from the normal series of patients, and no coccus resembling *Streptococcus subacidus* was found (Table I). Likewise, there is no predominance of gram-positive nonhemolytic streptococci in patients of the trichomonad-infested series. Hemolytic streptococci were recovered in 32.5 per cent of the normal patients and in only 29 per cent of the trichomonad vaginitis cases.

TABLE I. BACTERIAL FLORA OF THE HUMAN VAGINA

ORGANISM ISOLATED	NORMAL VAGINA (86 CASES)		TRICHOMONIASIS (104 CASES)	
	NO.	%	NO.	%
Aerobacter aerogenes	11	12.8	14	13.4
Aerobacter cloacae	2	2.3	0	0
Alcaligenes faecalis	7	8.1	5	4.8
Döderlein bacilli (diphtheroid rods)	46	53.5	51	49.0
Escherichia coli	28	32.5	32	30.7
E. coli, var. *acidilactici*	7	8.1	11	10.6
Gaffkya tetragena	3	3.5	4	3.8
Proteus vulgaris	12	14.0	12	11.5
Pseudomonas aeruginosa	7	8.1	5	4.8
Pseudomonas fluorescens	2	2.3	2	1.9
Sarcina lutea	9	10.4	8	7.7
Sarcina ureae	2	2.3	5	4.8
Staphylococcus albus	54	63.0	57	55.0
Staphylococcus aureus	14	16.2	19	18.2
Staphylococcus citreus	9	10.4	6	5.8
Staphylococcus sp., alpha-hemolytic	6	7.0	12	11.5
Staphylococcus sp., beta-hemolytic	11	12.8	16	15.4
Streptococcus pyogenes, beta-hemolytic	18	21.0	20	19.0
Streptococcus salivarius	10	11.6	10	9.6
Streptococcus nonhemolyticus	42	49.0	34	32.6
Vibrio, unclassified	2	2.3	5	4.8
Yeasts, saprophytic	14	16.2	22	21.1
Candida albicans (Monilia)	0	0	3	2.9
Misc. gram-pos. micrococci	6	7.0	12	11.5
Misc. gram-neg. micrococci	11	12.8	17	16.4
Misc. gram-neg. coccobacilli	14	16.2	24	23.0
Unclassified organisms	2	2.3	4	3.8

Hesseltine and co-workers[6] found no organisms suggestive of *Streptococcus subacidus* in their experiments on intravaginal trichomonad implantation. These authors further observed that the trichomonad vaginitis syndrome may be produced by inoculation of the human vagina with a bacteria-free culture of *Trichomonas vaginalis*.

The only organism common to all cases of vaginitis in the present series was the trichomonad. Data obtained from experiments demonstrating the effect of bacteria isolated from the human vaginal vault upon the growth of *Trichomonas vaginalis* (in vitro) will be published shortly.

Summary

Microorganisms in the human vaginal vault were isolated from 104 clinical cases of *Trichomonas vaginalis* vaginitis and are compared and contrasted with the microflora isolated from a control series of 86 normal patients without vaginal discharge or any clinically confirmable manifestations of a trichomonad infestation. The bacteria isolated in both series are strikingly similar in distribution both as to species and frequency of presence.

No single bacterial or fungus organism is associated with the flagellate, *Trichomonas vaginalis,* in clinical cases of vaginitis that does not appear in the normal vagina. Döderlein bacilli or diphtheroid rods appear to be present in a similar frequency in the trichomonad-infested vagina and the normal vagina. Common to all cases of trichomonad vaginitis in this series is the flagellate, *Trichomonas vaginalis.* These data would appear to support the contention that this trichomonad is the etiological agent in a specific vaginitis.

I am grateful for the cooperation of the Elmer Belt Urologic Group, Los Angeles, in providing clinical material for this study. Personal appreciation is expressed to Dr. Elmer Belt for providing grants-in-aid and to Drs. Gordon H. Ball and Meridian R. Ball for continued interest in the problem and comments on the manuscript.

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CONGENITAL CYSTS OF THE CORPUS UTERI

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CYSTS within the uterine musculature are uncommon lesions in gynecological practice. The only reference in the American literature to this problem, is a case report and review of the literature by Hamblen[1] of Duke University in 1936. Numerous case reports have appeared in the European literature, however, and Robert Meyer[2] devotes an entire chapter to the discussion of this problem. The objective of this paper is to present a case of an intramural uterine cyst containing a true epithelial lining and to discuss its etiology in the light of similar cases reported in the literature. We wish to call attention to the distinction between epithelium-lined intramural cysts of the uterus, which are thought to be of congenital origin, and such commonly known lesions of well-established origin as cervical retention cysts, cystic degeneration of myomas or adenomyomas, and serosal cysts. This last-named group of acquired lesions is not within the scope of this paper, except from the standpoint of differential diagnosis.

CLASSIFICATION OF UTERINE CYSTS

I. Acquired Cysts
   - A. Cystic degeneration of myomas
   - B. Cystic adenomyomas
   - C. Cervical retention cysts
   - D. Serosal cysts

II. Congenital Cysts
   - A. Wolffian duct cysts
   - B. Müllerian duct cysts

Acquired Cysts

When one is confronted with a cystic structure involving the uterus, first consideration must be given to the acquired group of lesions, because they are by far the more common of the two groups.

Cystic degeneration of myomas is frequent in occurrence and ordinarily offers no problem in diagnosis. Histologically the characteristic whorled appearance of smooth-muscle bundles is seen with varying amounts of fibrous tissue elements. The cyst cavity has no epithelial lining, but occasionally confluent myomatous nodules will show small epithelial inclusions between them which are derived either from the uterine mucous membrane or the serosa, depending on whether the myoma is submucous or subserous in location.

Cystic adenomyomas occasionally occur as solitary lesions, but usually are seen in association with a diffuse adenomyosis uteri. The contents of this type of cyst are made up of old blood and necrotic tissue elements and character-

istically have a chocolate or tarry color and a moderately thick viscosity. The lining epithelium closely resembles endometrium which may or may not respond to the cyclic influence of the ovarian hormones. These epithelial islands deep within the uterine musculature often show glandlike outpouchings and there are varying amounts of endometrial stroma below the gland epithelium. There is also a diffuse hyperplasia and overgrowth of the myometrium in association with the endometrial islands.

Cervical retention cysts are occasionally found deep in the musculature in the region of the cervix uteri. Frank[3] described a case of a subserous cyst low on the posterior wall of the uterus which he felt belonged to this group. These cysts have the characteristic tall, nonciliated columnar epithelium of the endocervical canal.

Serosal cysts also fit into the gross classification of uterine cysts. As the name implies, they are located on the serosal surface of the uterus and elsewhere throughout the peritoneal cavity. Their origin may be from nests of mesothelial cells in the serosa which become hollowed out, forming small cystic cavities, or from adhesions following pelvic inflammatory disease and the formation of small closed cavities.

Congenital Cysts

If a cyst in question does not fall into any of the previously mentioned categories, the congenital origin must be considered. The two theories of congenital origin which have the majority of cases in support of them are the origins from the Wolffian and Müllerian ducts. The origin from the mesonephros was considered by von Recklinghausen,[4] but Kossmann,[5] Meyer[2] and others do not believe that remnants of the mesonephros are found in the uterus either normally or pathologically.

Wolffian duct cysts are the more common of the two types. The Wolffian ducts in their atrophied form, as seen in the adult woman, course through the broad ligaments in a medial direction from the mesovarium. They follow along the lateral surface of the uterus below the insertion of the round ligaments and then along the lateral wall of the vagina. Anywhere along this course cysts may develop in rests of the embryonic Wolffian ducts, but they are most commonly seen in the lateral vaginal wall or on the lateral portion of the cervix. Portions of these ducts may actually be included in the lateral uterine wall. In this situation, they could form cysts surrounded by myometrium and containing an epithelial lining, which may be cuboidal, columnar, or even stratified squamous epithelium. Several such cases have been described and there is almost universal agreement in the literature that epithelium-lined cysts arising in the lateral uterine wall, particularly below the insertion of the round ligaments, have as their common origin Wolffian duct rests.

It is easy to understand how a duct which develops equally in embryos of both sexes in the undifferentiated state, and forms the genital excretory tract in the adult male, could leave behind rests of epithelium which at a later

date proliferate and become cystic. However, cysts developing in the midline, in the anterior, posterior, or fundic portions of the uterus, cannot be logically explained on this basis.

Müllerian duct cysts were first described by Kossmann[5] in 1897. However, he was of the opinion that the lesion in question was an adenomyoma rather than a true cyst of the uterus. In 1911, Frankl[6] reported a cyst the size of a child's head in the fundus of the uterus which was surrounded by myometrium and contained a clear yellow fluid. The lining was a single layer of ciliated columnar epithelium with basely placed nuclei. Frankl felt that the cyst arose from the invagination of the Müllerian ducts during embryonic development. He called attention to Meyer's work in which the latter author, in a series of fetal uteri, found numerous instances of islands of Müllerian-duct epithelium growing in the midline.

Meyer[2] reviewed the nineteen cases of uterine cysts reported up to 1930 and discussed at length the theories of origin. In Meyer's series, most of the cysts occurred in the midline. In half of his cases the cysts were found on the posterior wall or on the fundus of the uterus. In four cases, the cysts arose from the anterior wall, and, in one case, the cyst was on the cervix posteriorly. Half of the cysts in the reported cases were very superficial or pedunculated. In one case the cyst was parasitic, the only attachment to the uterus being through adhesion bands. The largest cysts were growing in the outer layers of the myometrium because in the inner layers of the myometrium the counter-pressure of the uterine musculature restricts their size. Some of these cysts have grown to the size of a term pregnancy. The lining epithelium in Meyer's series usually resembled endometrium, but in one case, that of Pribram's, the epithelium resembled that of the endosalpinx. The tall columnar epithelium was often found to be resting on a particular type of fibrillary connective tissue and was often thrown up into crests and depressions. It was Meyer's belief that most, but not necessarily all, uterine cysts are derived from Müllerian duct rests. He considered that certain of the laterally lying cysts could be derived from the Wolffian ducts. Meyer based his belief primarily on the finding that most of these cysts are found lying in the midline and also on his study of fetal uteri in which he found many examples of Müllerian duct rests, which closely resembled these cysts which develop later in life.

Since Meyer's classical review on this subject, cases have been reported by Maxwell,[7] Hawkins,[8] Hamblen,[1] Dubrausky,[9] Palmstierna,[10] and Treite.[11] Following the report of our case, these cases will be summarized and compared with Meyer's series.

Case Report

F. H., a 52-year-old gravida ix, para vi, was admitted on Jan. 27, 1953, with the chief complaint of vaginal bleeding of three days' duration.

The history obtained led us to believe that the patient had her menopause in July, 1952, at which time she had her last normal three-day menstrual period. In November, 1952, the patient spotted for two days and at the time of admission she had been bleeding heavily for three days, saturating about twelve to fifteen pads daily since the onset of the complaint.

Past history revealed that prior to admission she had been under medical care because of hypertension. For the past twelve months she had experienced slurring of speech and was ambulatory only with the aid of a cane. At the time of onset of the last episode of vaginal bleeding, she had been confined to a wheel chair and was unable to walk without assistance.

Physical examination on admission showed a well-developed, fairly well-nourished white woman with slurred, rather slow speech. The right eye showed a right lateral palsy, and there was a left facial weakness. The tongue deviated to the right on protrusion. The chest was essentially clear, while the heart was enlarged to the left side and demonstrated a Grade II systolic murmur in the mitral area transmitted to the neck and apex; the blood pressure was 206/104. Abdominal examination revealed the presence of a mass extending from the pubic symphysis to approximately one fingerbreadth below the umbilicus, nontender and regular in outline. No other organs or masses were palpable. On pelvic examination, this mass was thought to be uterine in origin and gave the impression of being cystic in nature. Both adnexal regions were negative and the cervix was clean on speculum examination.

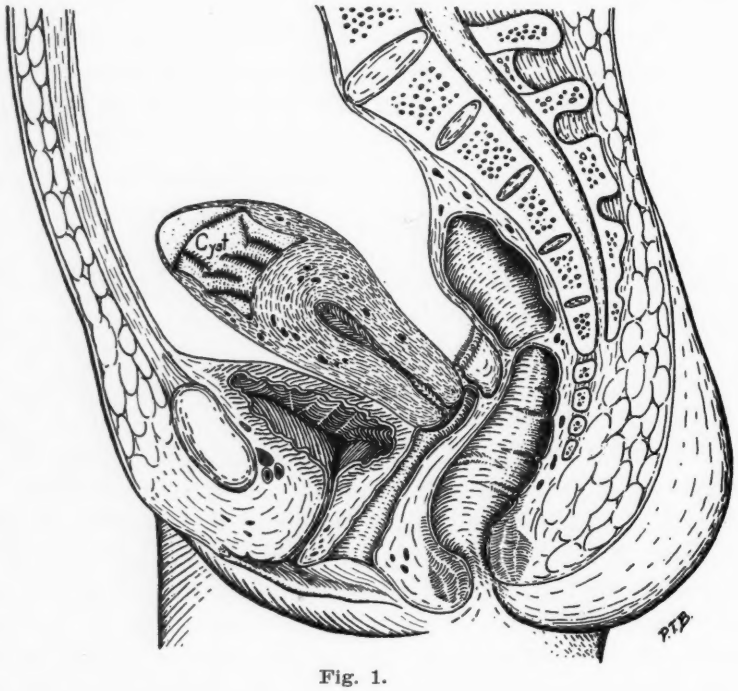

Fig. 1.

After medical investigation, revealing, among other things, an enlarged heart on chest x-ray and left ventricular strain on electrocardiogram, the patient was taken to the operating room, and a dilatation and curettage followed by panhysterosalpingo-oophorectomy were performed. When the peritoneal cavity was opened, a large mass the size of a 3½ month gestation was revealed in the lower abdomen. This mass was cystic and contiguous with the anterior surface of the fundus of the uterus. Both tubes and ovaries were of normal appearance. While the cystic mass, together with the uterus, was delivered into the abdominal incision, the thin-walled cyst ruptured with the escape of clear nonodoriferous serous fluid into the peritoneal cavity. The cystic cavity measured about 6 cm. in diameter, and had a fairly clean, broad base, without signs of recent bleeding. The operative procedure thereafter was uneventful, and the patient left the operating room in good condition.

The postoperative course was very stormy and the patient died on the fourth postoperative day, apparently from a recurrent cerebral accident. Consent for postmortem examination was refused by the family.

Pathological Examination.—

Gross description: (Dr. B. W. Juvelier) The specimen received was a totally resected uterus with adnexa attached which weighed 375 grams. The cervix measured 4.2 cm. in length. The portio vaginalis showed areas of hyperemia and erosion. The endometrium, measuring less than 0.2 cm. in thickness, showed the effects of scraping. The myometrium at its thickest portion measured 2.5 cm. and showed an occasional interstitial myoma which measured less than 0.5 cm. in diameter. Arising from the anterior surface of the fundus uteri in the midline was a funnel-shaped emptied cystic structure which had a small tear at its apex. Its base was formed by the uterine fundus and the muscular wall of the cyst was continuous with the myometrium of the anterior and posterior walls of the uterus, so that the cyst was intramural in location. The outer wall was covered by serosa which was continuous with the perimetrium. There were no adhesions around the uterus or cyst. The cyst was 5 cm. in depth from base to apex and was 4.5 cm. in diameter at its base. The cyst wall measured 1.3 cm. in thickness at the base and 0.2 cm. in thickness at the apex. The inner cyst wall showed gyrated protrusions laterally, but its base and apical portions were smooth. The inner wall of the cyst showed hyperemia. Here and there on the smooth surface small warty papillary projections could be seen which were tan in color. No communication could be demonstrated between the cavum uteri and the cystic cavity. See the reconstructed drawing Fig. 1, and the photograph of the opened cyst, Fig. 2. The Fallopian tube measured 13 cm. in length and the fimbriated end was open. Near the fimbriated end was a small pedunculated cyst. The ovary measured 3 by 3.3 by 1.1 cm. and on section showed yellow bodies. The other Fallopian tube measured 10.2 cm. in length. The fimbriated end was open and no thickening was noted. The ovary measured 4 by 3.2 by 1.2 cm. and contained a cyst filled with hemorrhagic fluid and small white bodies.

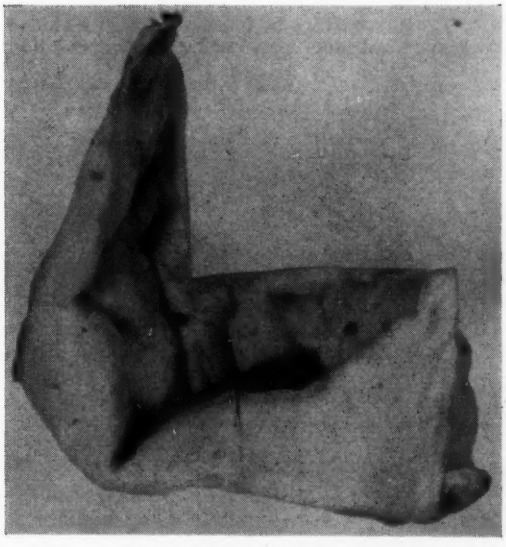

Fig. 2.—Sectioned uterine cyst showing gyrated protrusions laterally, and smooth base and apical portions.

Microscopic description: The cervix showed cystic dilatation of the glands. Several areas of squamous metaplasia were seen. There was a moderate dilatation of capillaries in the region of the squamocolumnar junction, with collections of small round cells and occasional neutrophils. There was marked thickening of arteries almost to obliteration.

The endometrium showed hemorrhages. The glands were in the proliferative phase and in some areas, the endometrium was extending into the myometrium showing thereby a slight degree of adenomyosis interna. Some endometrial glands were dilated. Blood vessels showed distinct thickening.

The cyst was covered by a thin layer of serosa. The wall consisted of smooth muscle which decreased in amount as the thin-walled apical portion was reached. There was a thin layer of fibrillar connective tissue underneath the mucosa which was hyalinized. The inner wall was lined by a single layer of tall, ciliated, columnar epithelium which showed areas of pseudostratification. The nuclei were large, vesicular, centrally placed, and usually contained one nucleolus. Many of the cells showed subnuclear vacuolization which

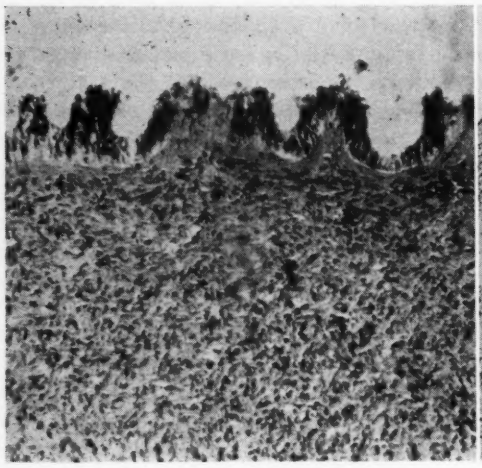

Fig. 3.

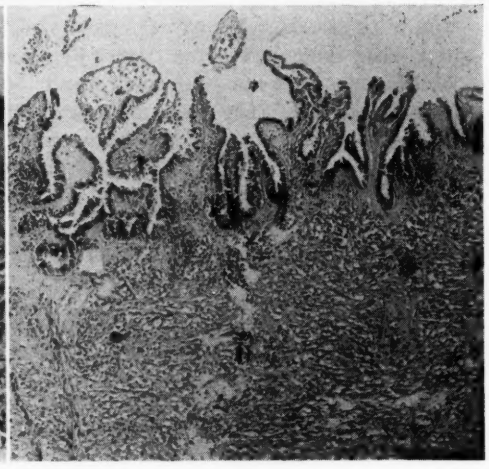

Fig. 4.

Fig. 3.—Low-power photomicrograph showing low tufts of epithelium projecting up from the surface.

Fig. 4.—Low-power photomicrograph showing distinctly papillary architecture.

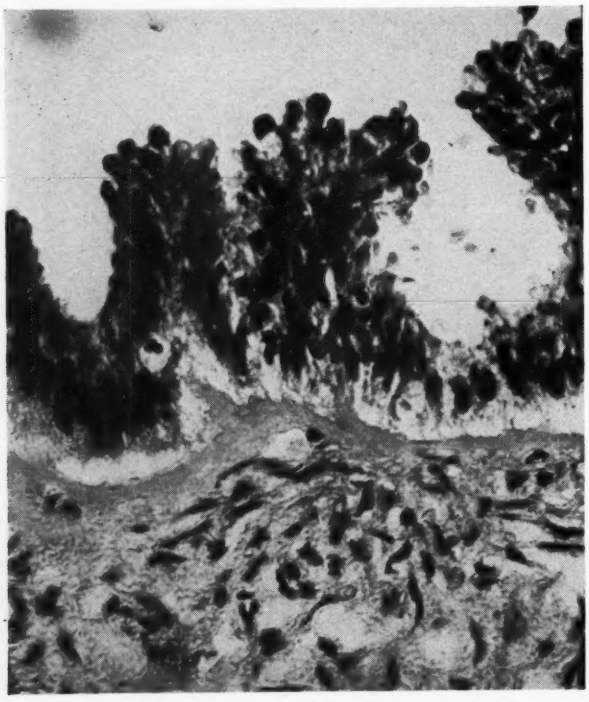

Fig. 5.—High-power photomicrograph showing pseudostratified tall columnar epithelium with subnuclear vacuolization and fibrillar submucosal layer.

was well demonstrated in the high-power photomicrograph, Fig. 5. The architecture of the epithelium varied considerably. In most areas it was flat with low tufts of epithelium projecting up from the surrounding epithelium (Fig. 3). In other areas, the architecture was distinctly papillary, the mucosa being thrown up into fingerlike projections giving it a polypoid appearance (Fig. 4).

The Fallopian tubes were not remarkable. One ovary showed a corpus luteum with hemorrhage and some follicle cysts. The other ovary showed many corpora albicantia.

Comment

We feel that the position of this cyst on the anterior surface of the uterus in the midline precludes the possibility that it could be of Wolffian-duct origin. The only other possibility to be excluded would be a cystic adenomyoma. The finding of a slight amount of adenomyosis in this case might seem to strengthen the case in favor of a cystic adenomyoma; however, on microscopic comparison of the endometrial islands and the epithelium of the cyst, they do not bear the slightest resemblance to each other. The ciliated columnar epithelium of the cyst resembles most closely the epithelium of the endosalpinx, although it would seem that the epithelium had not undergone complete differentiation from the primitive Müllerian-duct type. Therefore, on the basis of the midline position, the resemblance of the epithelium to primitive endosalpinx, and the similarity to other cases reported in the literature, we feel that this case represents a congenital cyst of Müllerian duct origin.

TABLE I. SUMMARY OF CASES REPORTED SINCE MEYER'S REVIEW, 1930

AUTHOR	TYPE	SIZE	LOCATION	EPITHELIAL LINING
Maxwell	Subserous	Orange-sized	Posterior wall	Cuboidal
Hawkins	Submucous	Volume 10 c.c.	Posterior wall	Ciliated columnar
Hamblen	Intramural	12 cm. in diameter	Posterior wall	Columnar
Dubrausky	Submucous	5.8 cm. in diameter	Anterior wall	Endometrium-like functional
Palmstierna	Pedunculated subserous	Size of a man's head	Posterior fundus	Ciliated columnar
Treite Case 1	Subserous	Size of a child's head	Posterior fundus	Ciliated columnar
Treite Case 2	Pedunculated submucous	Egg-sized	Presented at cervical os	Endometrium-like functional
Authors' Case	Intramural	5 cm. in diameter	Anterior fundus	Ciliated columnar

These eight cases bring the total number of cases reported in the English and German literature to twenty-seven and agree well in structural characteristics with Meyer's series of nineteen cases. There are certain important differences, however, which should be mentioned. Two new types have appeared, the submucous and the pedunculated submucous varities. One of the pedunculated submucous cysts presented at the cervical os as a polypoid structure. It is also noteworthy that half of these cases showed ciliated columnar epithelium, in contrast to Meyer's series in which only one case showed this type of epithelial lining. This could represent an attempt on the part of the primitive Müllerian epithelium to reproduce the endosalpinx. We feel that this emphasizes the multipotential nature of the epithelium involved and explains the variation in the type of epithelium found in these uterine cysts. Also of interest is Hamblen's case, which is the only example of this type of cyst reported in a pregnant uterus.

Summary

Congenital cysts of Müllerian-duct origin present a varied picture. The various anatomical types which have been reported are the pedunculated submucous, submucous, intramural, subserous, pedunculated subserous, and parasitic. Most common are the subserous or pedunculated subserous types. They are usually found in or near the midline. In about half of the cases they are found on the posterior wall of the uterus, but they may also be found on the fundus, anterior wall, or cervix. The cysts are most often found singly, but several cases of multiple cysts have been described. The lining epithelium may resemble endometrium, endosalpinx, or endocervical epithelium, or may be of a primitive Müllerian-duct type. The usually found columnar epithelium may show flattening due to the pressure effect from the expanding contents of the cyst. In places the epithelium may be missing. The epithelium is often found lying on a hyalinized layer of submucosa, and may be thrown up into ridges and papillary projections. The wall of the cyst is usually composed of smooth muscle with varying amounts of fibrous-tissue elements. No communication with the uterine cavity was demonstrable in any of the reported cases.

The average age of the patients in whom these cysts have been found is 36, and the age range is from 25 to 52 years of age. They occur more frequently in women who have borne several children. The symptoms are nonspecific, being those of a lower abdominal mass. The most frequent preoperative diagnosis is that of an ovarian cyst or myomas of the uterus. The treatment depends upon the size and location, and consists of either excision of the cyst or hysterectomy.

These cysts are generally considered to be benign in nature. Dworzak[12] described a case which he thought to be one of Müllerian-duct origin with malignant degeneration of the epithelium. However, the description of the case gives one considerable reason to suspect that he might be dealing with an interligamentary papillary cystadenoma of the ovary. A case of this type was later described by Fukushima,[13] in which metastasis from a previously removed papillary cystadenoma of the ovary gave rise to several uterine cysts which superficially resembled the type of cyst in question.

The generally adhered to theory of origin is the one first proposed by Kossmann and elaborated and established experimentally by Frankl and Meyer. This theory states briefly that the cysts are derived from the invagination of the Müllerian ducts as they grow together and fuse in the midline to form the fundus and body of the uterus.

Conclusions

1. A classification of uterine cysts has been proposed.
2. A case of an intramural epithelium-lined cyst of the uterus has been presented.
3. The literature concerning similar cases has been reviewed.
4. In our opinion, this case represents a congenital cyst of the uterus of Müllerian-duct origin.

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New Instruments, Etc.

PERFORATIVE APPENDICITIS WITH GENERALIZED PERITONITIS IN LATE PREGNANCY

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RENN, Douglass, and Cushman,[1] in 1951, reviewed the literature of the preceding 15 years and found only 15 reported cases of perforative appendicitis with generalized peritonitis as a complication of pregnancy at or near term. They presented two additional cases, and urged that all such cases be reported in order that additional data for statistical evaluation of treatment of a controversial subject might be accumulated. For a summary of the rationale and arguments for and against the various procedures reported, it is suggested that the paper of Renn and his associates be reviewed.

Report of Case

Mrs. C. B., aged 27 years, gravida iv, stillborn i, abortions ii, was admitted to this hospital on Dec. 24, 1949, at about 8 months' gestation. The date of her last menstrual period was not known. She was referred from another hospital where she had been attended for 2 days. A history was obtained of sudden severe abdominal pain on Dec. 21, followed by persistent vomiting, and slight vaginal bleeding. She had received opiates and intravenous fluids, but pain and vomiting continued, accompanied by abdominal distention and increasing weakness.

On entry, the pulse rate was 110 and temperature 98.4° F. The leukocyte count was 14,250 with 93 per cent polymorphonuclear leukocytes, 6 per cent lymphocytes, and 1 per cent monocytes. The urine was negative. Blood type was A, Rh negative, and the erythrocyte count was 3.55 million.

The general appearance was that of a critically ill patient, dehydrated, prostrated, and very uncomfortable. Blood pressure was 120/70. The abdomen was boardlike and extremely tender throughout, with marked epigastric distention. Fetal heart tones were audible. The cervix was thick and closed, not "ripe." A small amount of old blood was present in the vagina.

A diagnosis of an acute obstetrical emergency, either abruptio placentae or peritonitis, was made, and the patient immeditely taken to the operating room after an intravenous infusion.

A low midline incision was made, and foul pus was encountered on opening the peritoneum, with no evidence of localization. Peritonitis was generalized as a result of a necrotic appendix, perforated near the base. A low cervical cesarean section was

done with cephalic delivery of a viable premature 4 pound infant. The appendix was removed and hysterectomy contemplated, but decided against because of the gravity of the general condition of the patient. One hundred mg. of aureomycin in solution was instilled in the peritoneal cavity, and the abdomen closed without drainage.

The pathological diagnosis was acute gangrenous appendicitis with perforation, fecal concretion in lumen, fibrinopurulent periappendicitis, and normal placenta.

After surgery, Wangensteen drainage was instituted and 2.5 Gm. of sulfadiazine was given intravenously in 1,000 c.c. of 5 per cent glucose solution. One Gm. of aureomycin was given intravenously between 6 and 20 hours postoperatively; 50,000 units of penicillin was given intramuscularly every three hours for 9 days. A total of 1,000 c.c. of whole blood and 8,000 c.c. of glucose solutions were given.

The temperature rose to 102.2° F. on the first postoperative day, then steadily declined to normal on the third day, after which it remained normal except for daily rises to 100° F. on the seventh and eighth days. There were no chills. On the third postoperative day, the abdomen was soft, good results of flatus and feces were obtained with a low enema, the Wangensteen drainage was discontinued, and the patient allowed oral feedings. The entire postoperative course was smooth and uneventful. Skin sutures were removed on the eighth day, and the wound healed per primam. She was discharged on the eleventh day.

It is of interest that regular menstrual cycles were soon established, and that conception occurred again about one year later. In a follow-up letter, her family physician reported to us that she had an early abortion in March, 1951.

The table of results presented by Renn and co-workers, with the addition of this case, is reproduced in Table I.

TABLE I. OUTCOME IN CASES NOTED IN THE LITERATURE

PROCEDURE	NO. OF CASES	FETAL DEATHS	PER CENT	MATERNAL DEATHS	PER CENT
1. Appendectomy only (permitting spontaneous onset of normal labor)	11*	3	27.3	1	9.1
2. Appendectomy and cesarean section	3	0	0	0	0
3. Appendectomy and hysterectomy	2†	0	0	0	0
4. Appendectomy and manual dilatation of cervix	2‡	0	0	0	0
Total	18	3	16.66	1	5.55

*Appendectomy followed delivery in one case.
†One subtotal and one total hysterectomy.
‡Prepartum appendectomy in one and postpartum in other.

Greenhill[2] states that, "In view of the high mortality of suppurative appendicitis at or near term, perhaps it would be best, in the interests of two individuals, to remove the appendix and do a cesarean hysterectomy at the same time. Not enough cases are on record to settle the point definitely, but simple cesarean section is certainly contraindicated." It seems that with such potent therapeutic adjuncts as modern antibiotics, re-evaluation of some surgical dictums and principles might be indicated. One such example is the proved lowered mortality since the abandonment of surgical wound drainage in peritonitis. We feel that, with antibiotic drugs, one may be allowed, under peculiar individual circumstances, more latitude in the method of handling peritonitis in pregnancy. Though the total number of reported cases is still small, we cannot ignore the 27.3 per cent fetal mortality in the simple appendectomy group; nor can the absolute sterility resulting in the hysterectomy group be lightly dismissed.

We are not advocating appendectomy and cesarean section in peritonitis, but merely presenting a case so handled for its statistical value.

We, frankly, held little hope for this mother's recovery at the time of operation. Because of the gravity of her condition and the fact that she was childless, we were perhaps influenced to make a case on behalf of the infant, against better surgical judgment; likewise, we did not feel that she could stand the additional insult of hysterectomy.

Conclusions

A case of perforative appendicitis with generalized peritonitis and pregnancy near term, successfully treated by appendectomy and cesarean section, is reported.

This method of treatment is not recommended as the one of choice, but is reported for statistical value.

All cases of generalized peritonitis from perforated appendicitis in late pregnancy should be reported, regardless of method of treatment or outcome, in order that more data may be accumulated for evaluation of treatment.

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GRANULOMATOUS PERITONITIS SECONDARY TO PERFORATION OF DERMOID CYST*

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GRANULOMATOUS peritonitis is a rare condition, usually resulting from perforation or rupture of an ovarian dermoid. Dermoid cysts themselves are not infrequently encountered in gynecologic practice, inasmuch as they comprise 10 per cent of all ovarian cysts; nor are torsion and/or rupture of other ovarian growths unusual occurrences. However, the perforation or rupture of an ovarian dermoid is unusual, since this type of growth is so thickly encapsulated.

Quer, Dockerty, and Mayo[1] have recently reported an extensive review of the literature; they found only 30 cases of intraperitoneal rupture and 8 of perforation into a neighboring viscus (rectum). They reported one additional case of granulomatous peritonitis. Among the 400 patients operated upon for dermoid cysts at Mayo Clinic, they found only 4 cases of rupture, 2 of which were complicated by granulomatous peritonitis. In our review of the literature, we were able to find only one additional case[2] and wish to report the following case of our own:

The patient was a 31-year-old white woman, gravida ii, para ii, who was referred by her family physician because of a rapidly growing pelvic tumor and weight loss. She had been attended by the senior author for her first pregnancy in 1946. The pregnancy was uneventful except for complicating uterine fibroids. At 42 weeks of pregnancy, she was admitted to Michael Reese Hospital for elective cesarean section. The indications were postmaturity, failure of engagement of the presenting part, and uterine myomas. X-ray examination on the day of surgery revealed a normal term infant and showed the left half of the pelvis to contain a "peculiar irregular dense shadow that suggests the possibility of a calcified myoma of moderate size." A low cervical cesarean section was performed and a normal infant delivered. A myomatous tumor measuring 0.5 by 4 cm. was removed from the anterior wall of the uterus and no additional growths were found. We do not routinely inspect the ovaries at low cervical cesarean section and, in this instance, we felt that the myoma which we removed accounted for the shadow seen on the x-ray films. The patient made an uneventful postoperative recovery and postpartum examination revealed an apparently normal status.

From 1947 on, the patient was treated by a dermatologist for chronic discoid lupus erythematosus of the face. In 1949, she was admitted to the hospital at the thirty-ninth week of pregnancy for a repeat cesarean section. A normal infant was delivered. No uterine myomas were found. The patient made an uneventful recovery and the postpartum examination was negative.

In November, 1951, she was referred back to the senior author by her family physician because of a rapidly growing pelvic tumor. She gave a history of normal regular menstruation and stated that, since May of 1951, she had had intermittent, sharp rectal pain.

*Presented at a meeting of the Chicago Gynecological Society, April 17, 1953.

In addition, she had an attack of pain in the right lower quadrant in August which lasted for ten days. Her family physician had made a provisional diagnosis of cholecystitis but x-rays of the gall bladder were entirely negative. The patient had lost 30 pounds over a period of 3 months despite a good appetite and had been running a low-grade fever for one month prior to our examination.

Physical examination revealed a 31-year-old white woman who appeared in no acute distress. There was a scarred butterfly-pattern dermatitis of the face. There was a firm mass in the abdomen extending midway between the pubis and umbilicus which appeared to be semicystic and moderately fixed. The uterus was normal in size and was anterior to the cystic mass. X-ray of the chest was negative. The hemoglobin was 13.4 Gm., the white blood count, 5,150 and the differential count normal. The sedimentation rate was elevated to 43 mm. in one hour. The patient was admitted to Michael Reese Hospital with a diagnosis of possible carcinoma of the ovary.

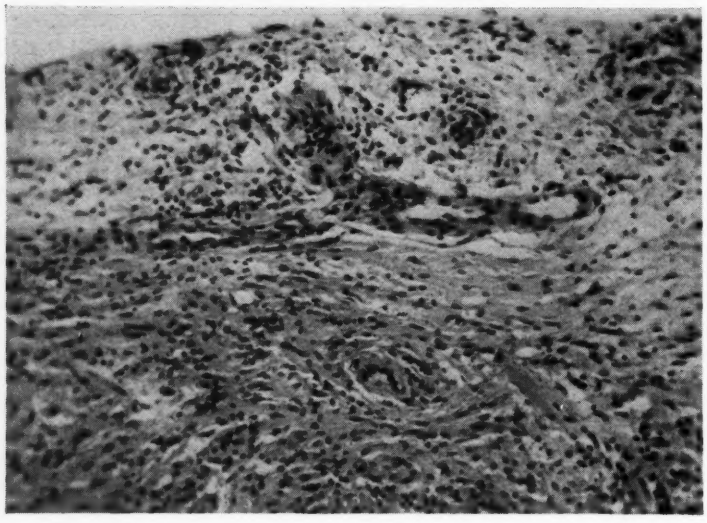

Fig. 1.—Microscopic section of peritoneal granuloma. Note giant cells.

Laparotomy was performed on Nov. 30, 1951. Upon opening the abdomen, a thick, friable omentum was found densely adherent to the anterior abdominal wall, grossly resembling extensive involvement by carcinoma. The omentum was separated with difficulty and the pelvis was explored. A large dermoid cyst of the left ovary was found completely filling the true pelvis and adherent to surrounding viscera. The right ovary was replaced by a hemorrhagic endometrial (chocolate) cyst, similarly adherent. The uterus was on top of, and firmly adherent to the dermoid. Further exploration revealed adhesions and numerous 0.5 to 2 cm. nodules scattered over the bowel, mesentery, omentum, liver, gall bladder, and parietal peritoneum. Macroscopically, the nodules had the gross appearance of caseous tuberculosis. Because of the extensive pelvic involvement and apparent tuberculous peritonitis, total abdominal hysterectomy, bilateral salpingo-oophorectomy, and lysis of adhesions were performed. The patient had a fairly stormy course for 4 days with elevation of temperature to 102.4° F. She was placed on streptomycin postoperatively because of the provisional diagnosis of tuberculosis but there was no effect until penicillin was added. Recovery was then rapid and uneventful and she was discharged on the ninth postoperative day.

Pathological examination of the specimen revealed the following: dermoid cyst, simple, and corpus luteum cysts of the left ovary; endometrial cyst of the right ovary with organizing perioophoritis; chronic endocervicitis with old erosion and Nabothian cyst; chronic peritonitis with organizing inflammation of fat. *There was no evidence of tuberculosis or malignancy.*

The final diagnosis was granulomatous peritonitis with involvement of the liver, gall bladder, bowel, omentum, parietal peritoneum, and pelvic organs, secondary to perforation of a dermoid cyst.

Summary

Rupture or perforation is a rare complication of ovarian dermoid cysts, having been reported in the literature as occurring in 0.5 per cent to 4.5 per cent of cases. When granulomatous peritonitis is found at laparotomy, there is no advantage in attempting the removal of the widespread nodules already present as a result of the spill of the irritating fatty contents of the dermoid. Removal of the dermoid prevents the appearance of new adhesions and peritoneal granulomas. Since granulomatous peritonitis grossly presents a picture similar to that of carcinomatosis and/or extensive tuberculous peritonitis, it is essential that a microscopic examination be made for accurate differential diagnosis.

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TRANSABDOMINAL ENCEPHALOCENTESIS IN A CASE OF CONGENITAL HYDROCEPHALUS*

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THE following case is presented to illustrate a little-used technique in the management of hydrocephalus.

A 24-year-old Negro woman, gravida iv, para iii, entered the labor rooms of Cook County Hospital on March 12, 1953, with a history of spontaneously ruptured membranes two hours prior to admission. During the course of her pregnancy she had been attending a Board of Health prenatal station, and her record from there was essentially normal.

Initial examination revealed the bag of waters to be ruptured, the cervix thick, and 1 to 2 cm. dilated, a breech presentation at minus 2 station. Fetal heart tones were 140 and regular. No uterine contractions were present. Abdominal palpation revealed a large globular mass which occupied the entire fundus and to which the uterus was closely applied. Impression was that the fetus had a hydrocephalus. The patient was sent for x-rays, which revealed a huge hydrocephalus and breech presentation (Fig. 1).

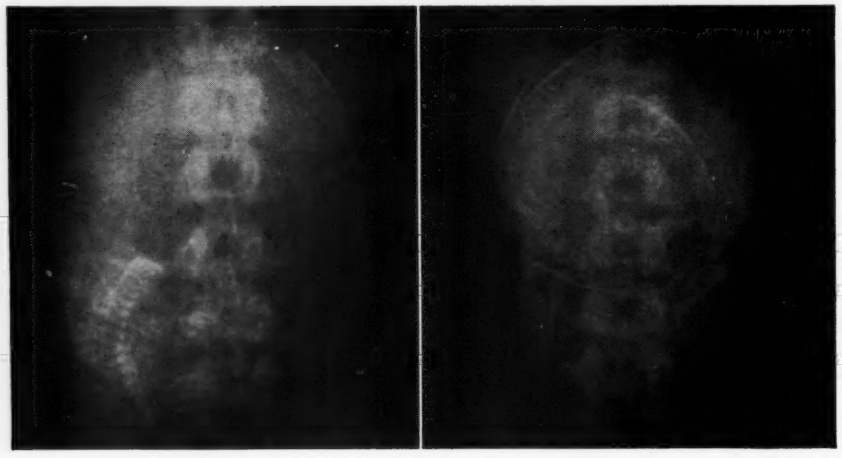

Fig. 1. Fig. 2.

Fig. 1.—X-ray before transabdominal encephalocentesis.
Fig. 2.—X-ray immediately following this procedure.

A modification of the transabdominal procedure, which had been suggested by Wilson[1] in 1937, was decided upon. The three most frequent maternal complications of hydrocephalus, as enumerated by Crenshaw and Banner[2] are (1) rupture of the uterus, (2) postpartum hemorrhage, and (3) postpartum morbidity. It was felt that these could be minimized by performing a transabdominal encephalocentesis prior to the onset of labor.

*Presented at a meeting of the Chicago Gynecological Society, April 17, 1953.

The patient was given 100 mg. of Demerol preoperatively. Catheterization was performed, and a sterile vaginal examination revealed the bag of waters to be ruptured, the cervix 50 per cent effaced and 2 cm. dilated, station of the breech minus 2, fetal heart tones 140. No uterine contractions were observed. The placental souffle was localized in the left lower quadrant.

The patient was then placed in sitting position and the abdominal wall was prepared. A point in the midline 3 cm. above the umbilicus was selected as the puncture site. The area was checked for bowel sounds, but none were present. This area was infiltrated with 1 per cent procaine solution. A 15 gauge spinal needle with the stylet in place was introduced through the anterior abdominal wall until resistance was encountered at a distance of about 4 cm. Slight additional pressure was sufficient to penetrate the fetal skull, and enter the cranial vault. The stylet was removed and clear cerebrospinal fluid was obtained under pressure. The head was allowed to decompress slowly. The fluid was checked for albumin which was found to be 3 plus.

Drainage continued for 30 minutes, during which time 2,500 c.c. of fluid was obtained. The McDonald measurement decreased from 40 cm. to 30 cm. following the tap. Fetal heart tones were 140 and regular. The patient was taken to x-ray (Fig. 2). At this time she began having mild labor pains, a phenomenon which we have frequently noted following transabdominal uterocentesis for cases of acute polyhydramnios.

Upon her return from x-ray, she was having strong uterine contractions every 3 minutes. Fetal heart tones at this time were 120 and regular.

Fig. 3. Fig. 4.

Fig. 3.—Before cerebrospinal fluid was replaced.
Fig. 4.—After 2,000 c.c. of fluid had been replaced.

The patient was again taken to the delivery room, where 30 minutes after the onset of labor she spontaneously delivered a full-term female hydrocephalic infant from the right sacral posterior position. The aftercoming head followed the shoulders without delay or difficulty (Fig. 3). No fetal heart tones were detected after delivery. The placenta was expelled 5 minutes after delivery and the blood loss was estimated at 150 c.c. Intravenous and intramuscular Ergotrate solution was given prophylactically. The cervix and the perineum were inspected and found to be intact. Her highest postpartum temperature was 98.8° F. and she was discharged on the fifth postpartum day.

As a matter of interest, an attempt was made to replace the fluid after delivery. After 2,000 c.c. had been replaced, technical difficulties, in the form of leakage, arose and the procedure was abandoned (Fig. 4). Measurements taken with four-fifths of the fluid replaced were as follows: circumference 60 cm., suboccipito-bregmatic 18 cm., biparietal 16 cm., occipitofrontal 20 cm.

The birth weight was 8 pounds, 8 ounces, without the cerebrospinal fluid which, if added, made the intrauterine weight of the infant 14 pounds.

Autopsy findings: Agenesis of pons and cerebellum. Internal hydrocephalus.

Summary

A case report illustrating a technique for the management of a hydrocephalic infant in breech presentation is discussed.

We felt that by means of this technique, the restoration of uterine tone would initiate labor and shorten the first and second stages, as well as minimize the most common maternal complications of hydrocephalus, i.e., ruptured uterus, postpartum hemorrhage, and postpartum morbidity.

Technically the procedure was easier and much less traumatic than many cases of craniotomy on aftercoming heads.

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DOUBLE UTERUS WITH DOUBLE PREGNANCY*

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THE literature on the subject of double uterus is very extensive and a great deal is being written about it currently. The term "double uterus" is being applied to any condition resulting from the failure of complete fusion of the Müllerian ducts. Thus it includes septate uterus, bicornuate uterus, uterus unicornis with rudimentary horn, double cervix, septate vagina, as well as uterus didelphys. However, true double uterus or complete uterus didelphys should apply only to a case of complete lack of fusion of the Müllerian ducts resulting in a double uterus, double cervix, and double vagina. Each uterus, of course, has only one tube and there are only two ovaries. It is with this type of double uterus that the present report is concerned.

Most of the authors discussing the subject of complete double uterus describe instances of pregnancy in one of the uteri and the complications that may arise as a result of this anomaly.

During the first trimester there may be vaginal bleeding of varying degree. This bleeding usually comes from the nonpregnant uterus which may increase to two or three times its normal size. If this bloody discharge is examined, decidual tissue will be found. Abortions, premature labor, abruptio placentae, premature separation of the placenta, and eclampsia are among the other frequent complications. There is also a greater incidence of breech and transverse presentation.

During labor maternal exhaustion, fetal embarrassment, prolonged first stage of labor, dystocia, and even rupture of the uterus may occur. Inertia may be caused by poorly developed uterine musculature. The nongravid uterus may become impacted in the pelvis and interfere with normal vaginal delivery. Then, again, the nongravid uterus may develop a hematometra or pyometra and interfere with the normal progress of labor. The vaginal septum may block the passage of the presenting part, requiring interference.

During the third stage of labor postpartum hemorrhage, retained placenta, and adherent placenta may occur.

Hoffman[1] states that, in the presence of uterus didelphys, it is more conservative to do an elective cesarean section than to subject the patient to unnecessary risks. However, most of the authorities agree that each case must be treated individually and, whenever possible, a trial of labor should be given. Uncomplicated deliveries do occur in many cases.

None of the authors who discussed the subject described any cases of double uterus with pregnancy in both uteri which he personally delivered.

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DeLee[2] mentioned one case which he saw in the eighth month of pregnancy, but labor was conducted by another practitioner.

Miller,[3] in a report of 55 cases from the literature and one of his own, mentioned that in seven instances it occurred in both uteri, but has no further details on the subject.

Frank R. Smith,[4] in a most extensive study of the subject, reported 35 cases of incomplete fusion of the Müllerian ducts that he collected from the records of 141,946 consecutive pregnant patients in the New York Lying-In Hospital from January, 1899, to July, 1930. Out of these cases, uterus didelphys occurred once in 28, 389 cases. In this entire series there was only one case of double pregnancy in a uterus didelphys which would put the incidence of this condition at one in 142,000.

It is evident, then, that double pregnancy in a double uterus with a successful outcome is comparatively rare. It is true that some of these cases may not be recorded or the presence of this condition may remain unrecognized. The case described here reached the lay press. Following this news item, reports began to pour in from various parts of the country, as well as from Japan, claiming the occurrence of similar cases.

Case Report

O. K., a 29-year-old white woman, presented herself in March, 1951, with a complaint of prolonged menstrual bleeding and sterility. Her menses started at the age of 13, occurring every twenty-eight days, and lasting four to five days. For the last seven to eight months she had been staining off and on for eight to ten days following her regular menstrual flow. She had been married for two years and never practiced contraception.

Vaginal examination revealed the vagina to be divided by a septum which ran anteroposteriorly from the vault of the vagina to about 5 cm. above the vaginal introitus. The septum was pulled over to the right side, so that the examining fingers first entered the left side of the vagina. The cervix was distinctly palpable on the left side. Upon introducing the examining fingers to the right of the septum another cervix was felt. The body of the uterus could not be definitely outlined.

Roentgenographic studies in March, 1951, showed the presence of a complete uterus didelphys; both tubes were patent and there was evidence of the possible presence of endometrial polyps. (Figs. 1 and 2).

It was evident from the vaginal examination that coitus was being had only in the left half of the vagina and the semen reached only the left uterus. It was considered of some advantage to make it possible for the semen to reach both cervices. With that in view, the patient was operated upon on May 15, 1951, the twenty-second day of her cycle. The operation consisted of a division of the vaginal septum and a dilatation and curettage of each uterus. The pathological report of the curettings of both uteri showed a glandular hyperplasia of the endometrium in the late proliferative phase with beginning secretory activity (Figs. 3, and 4).

Following the curettage, the patient continued to stain on and off though not as actively as before. She was given small doses of thyroid and in the second half of the cycle progesterone, 30 mg. daily, was given orally. There was no improvement in her condition.

According to the Hebrew law, no coitus is allowed for seven days following any bleeding or staining. This patient, being very devout, would have intercourse only beginning with the twentieth or the twenty-second day of her cycle. In the hope of

preventing the vaginal staining, the patient was placed on 6 mg. diethylstilbesterol 3 times daily, beginning with the fifth day of the cycle which started on May 30, 1952. She did not stain that month and coitus was presumably had from the twelfth day of the cycle. The medication was continued for thirty days. There was no period in June and July. On August 8, the patient stained slightly. An Aschheim-Zondek test taken on the following day was positive for pregnancy.

The antepartum course was uneventful. It was noticed that both uteri were developing and enlarging at the same rate and the presence of a pregnancy in each uterus was strongly suspected. On Dec. 16, 1952, x-ray examination revealed a pregnancy in both uteri. The fetus in the left uterus had a cephalic presentation while the one in the right had a breech presentation (Fig. 5). On Jan. 29, 1953, a repeat x-ray examination showed the same general picture except that the presenting head of the fetus in the left uterus was definitely dipping into the pelvic inlet. There was a slight trace of albumin in the urine but there was no edema and no elevation in blood pressure which varied between 112/80 and 124/85. There was no excessive gain in weight.

Fig. 1.

Fig. 2.

Fig. 1.—Roentgenogram of left uterus after administration of 8 c.c. of oil. The tube is well outlined with evidence of patency.

Fig. 2.—Roentgenogram of both uteri after administration of 8 c.c. of oil into right uterus. The tube of the right uterus is also well outlined with evidence of patency.

Since there was no cephalopelvic disproportion, no evidence of toxemia, nor any other complication, it was decided to allow this patient to have a test of labor and interfere only in case of any difficulty that might arise during labor. The alternative, delivery by cesarean section, as advocated by many authorities, was considered hazardous in this case. It would require operating first on one uterus, removing the fetus and placenta and closing the uterine wound, and then starting anew on the other uterus. The welfare of the second baby would have been jeopardized in case of a prolonged or delayed surgical procedure.

On Feb. 19, 1953, about three weeks before her expected date of delivery, the patient went into labor and was admitted to the hospital at 4 A. M. She was having pains every 4 to 5 minutes; her blood pressure was 114/80; fetal heart sounds were audible on both sides. Rectal examination revealed the cervix to be 2 cm. dilated and effaced. The presenting part was at zero station and the membranes were ruptured. Both uteri seemed to harden and tighten during the pains. At 6:30 A. M. the cervix was 5 to 6 cm. dilated and the presenting part was at plus 2 station. At 6:55 A. M. she was taken to the delivery room. Upon vaginal examination the cervix was found to be fully dilated, the

Fig. 3.

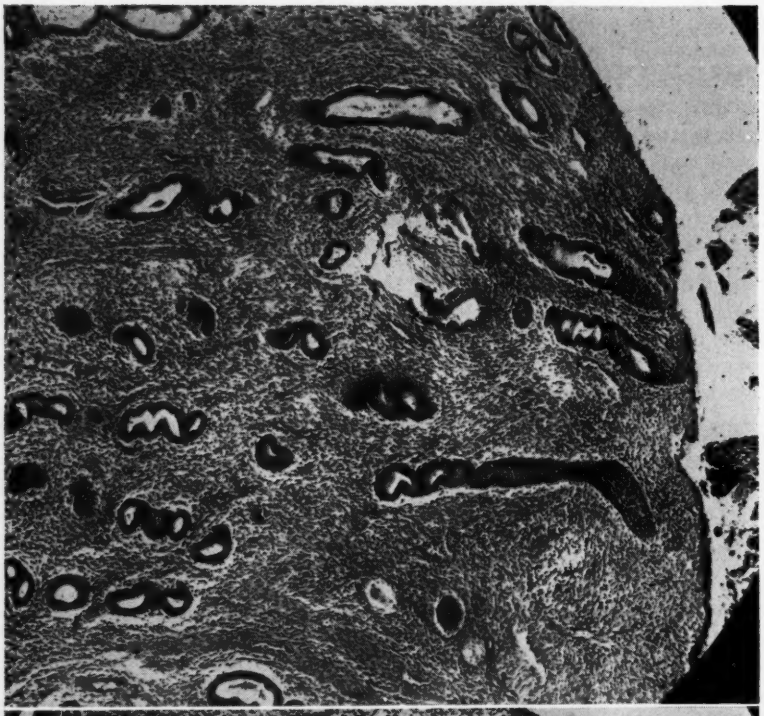

Fig. 4.

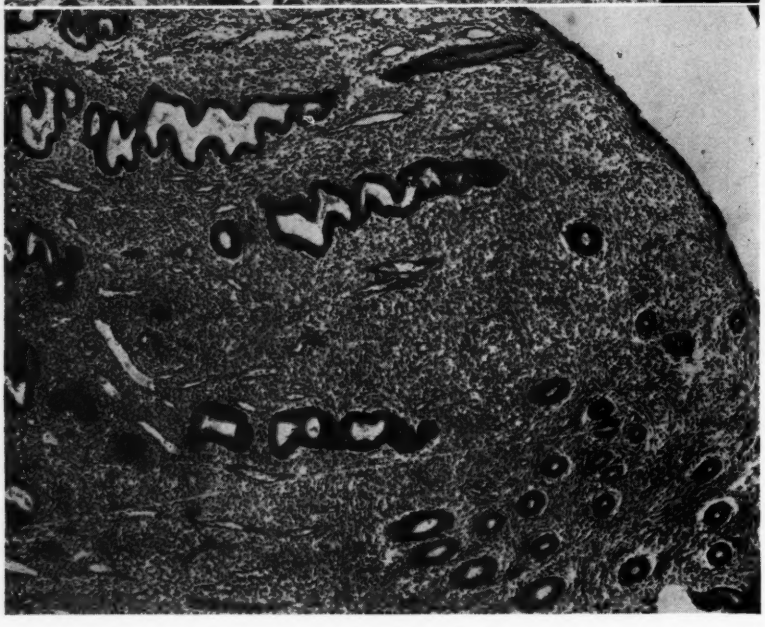

Fig. 3.—Low-power study of endometrial curettings of left uterus. The endometrium is in the late proliferative phase. The glands are slightly tortuous. Epithelial nuclei are at the base of the cells. There is no evidence of secretion in the lumen on the glands.

Fig. 4.—Low-power study of endometrial curettings of the right uterus showing essentially the same findings as in the endometrium of the left uterus.

head in left occipitotransverse position at plus 2 station. Under pudendal block anesthesia a right mediolateral episiotomy was performed. The head was rotated manually from left occipitotransverse to left occipitoanterior; low forceps were applied and a male fetus weighing 2,050 grams (4 pounds, 8 ounces) was delivered at 7:30 A. M. The infant was normal, in good condition, and had a prompt cry. The placenta and membranes were delivered five minutes later. No oxytocic was administered. There was no excessive vaginal bleeding. Vaginal examination at this time revealed that the baby was delivered from the left uterus which was now hard, well contracted, the height of the fundus being at about two fingerbreadths below the umbilicus. The cervix of the right uterus was found to be 3 cm. dilated, not fully effaced. The membranes were intact. The presenting part was above the pelvic brim but did not feel like a breech. The patient's condition was good. There were no labor pains and no uterine contractions could be detected upon holding one's hand over the uterus. The fetal heartbeat was heard over the right lower quadrant.

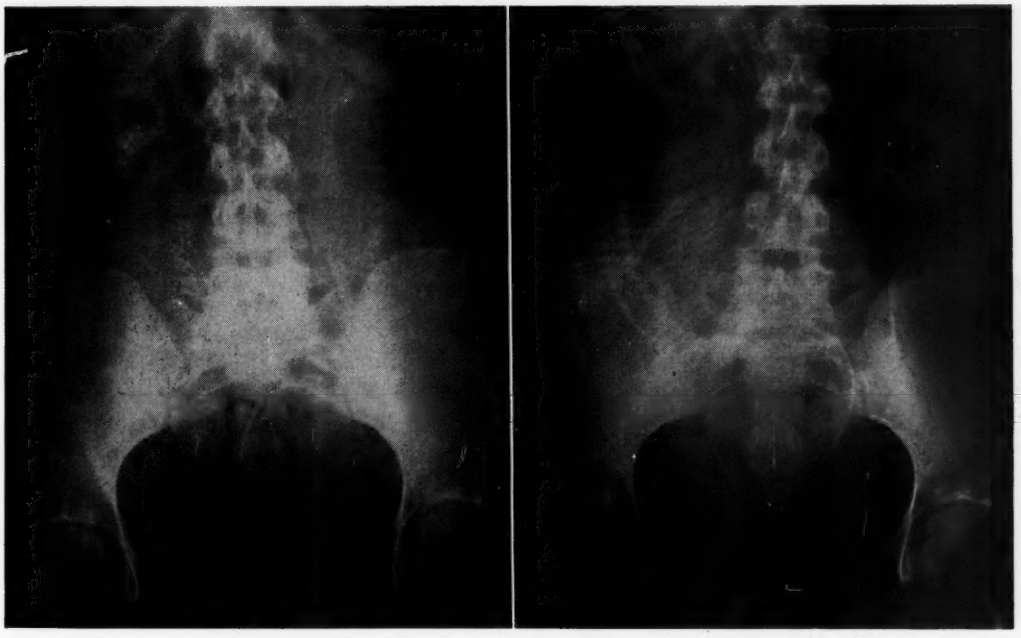

Fig. 5. Fig. 6.

Fig. 5.—Roentgenogram of patient in twenty-eighth week of pregnancy showing pregnancy in both uteri. The one in the left has a cephalic presentation while the one in the right has a breech presentation. Note that the fetuses are far apart from each other.

Fig. 6.—Roentgenogram of patient after delivery of infant from left uterus. Notice that the infant in the right uterus turned spontaneously from a breech into a cephalic presentation.

Hemostasis of the episiotomy wound was secured by clamping and tying the bleeding points.

The patient was then x-rayed. The roentgenogram showed the presentation to be cephalic (Fig. 6). The fetus then had turned spontaneously from a breech to a cephalic presentation some time between January 29, the date of the last x-ray examination, and February 19.

Labor stopped completely and the patient was removed to the labor room. Since the presenting part was floating it was considered risky to rupture the membranes at this time for fear of causing a prolapse of the cord. Intravenous Pitocin, 4 mg. to 500 c.c. of glucose in water, was administered at the rate of 40 drops per minute. The uterus con-

tracted irregularly but no real labor was initiated. The intravenous Pitocin was discontinued at 1 P. M. The patient's condition remained unchanged until 7 P. M. A vaginal examination at this time showed that the cervix had dilated up to 4 cm. and was practically effaced.

The presenting part was dipping into the pelvic brim. The condition of the cervix being more favorable, and the presenting part being in the pelvis, it was considered safe to rupture the membranes at this time. This was done, and intravenous Pitocin was started again at 7:30 P. M. The patient began to have strong pains and at 8:30 P. M. they were occurring every 3 to 4 minutes. The Pitocin was then discontinued. Labor progressed rapidly. At 10:30 P. M. the cervix was 5 to 6 cm. dilated, the head at zero station in the right occipitotransverse position. Caudal anesthesia was then started. At 11:30 P. M. the cervix was fully dilated. The patient was taken to the delivery room. The head was rotated manually from right occipitotransverse to right occipitoanterior; low forceps were applied and a male fetus was delivered, in good condition, that weighed 2,200 grams (4 pounds, 14 ounces). The placenta and membranes were delivered 5 minutes later. The episiotomy was repaired and mother and babies left the delivery room in good condition.

The postpartum course was entirely uneventful and the mother and babies were discharged 6 days later.

Comment

This case presents several interesting features. The reason for the pregnancy occurring in only one of the uteri, in cases of true uterus didelphys, may be due to the fact that one of them is underdeveloped to a degree sufficient to render gestation in it impossible. Another plausible cause of the pregnancy occurring in one uterus is the presence of the double vagina. The septum apparently divides the vagina in such a way that coitus is had in only one-half of the vagina, and the patient as well as the husband is usually unaware of the presence of a double vagina. The semen comes in contact with the cervix of only one of the uteri and it is in that uterus that pregnancy takes place.

Schauffler[5] described one case in which the husband was aware of the presence of a septum and was having intercourse on either side. In such an instance, superfetation is theoretically possible and cases were described in which the delivery from the two uteri took place weeks, days, and even months apart. When the partition of the vagina is eliminated, by dividing the septum, the cervix of either uterus is rendered equally accessible to the semen so that pregnancy may take place in either or both of them. The division of the vaginal septum in the case reported here may have been the contributing factor to the pregnancy occurring in both sides.

It is also interesting to speculate as to the mode and time of fertilization in each uterus. Judging by the size of the infants and the comparatively short interval between the delivery of these, one would be justified in supposing that gestation in both uteri took place during one single cycle. There were evidently two ova involved. If so, one is likely to wonder whether the two ova originated from the follicles of one ovary or whether ovulation took place in both ovaries during the same cycle.

Each uterus, in a uterus didelphys, is presumably narrower and less roomy than a normal single uterus. Yet, the fetus in the right uterus, larger

than the one in the left, managed to turn spontaneously from a breech into a cephalic presentation.

It is interesting to note, as far as labor is concerned, that the stimuli which initiate labor did not affect both uteri in the same manner. Only one uterus, the left one, went into full labor while in the other one labor progressed but slightly, in spite of the fact that it contained a larger fetus. This substantiates the idea that there must exist intrinsically in the uterus some condition which renders it either responsive or refractory to the stimuli that initiate labor.

Summary

1. A case of uterus didelphys is reported. The patient presented a problem of sterility which was presumably corrected by dividing the vaginal septum and by administration of hormonal therapy.

2. Pregnancy took place in both uteri during the same cycle.

3. One fetus turned spontaneously from a breech to a cephalic presentation some time during the last twenty-one days of pregnancy.

4. Labor started spontaneously in the thirty-eighth week of gestation.

5. Delivery of both infants was through the vaginal route, the one from the left uterus being born first and the other from the right being born fourteen hours later. Labor in the right uterus had to be initiated by rupture of the membranes and administration of intravenous Pitocin.

6. It is suggested that one of the causes of the pregnancy occurring in only one of the uteri in cases of uterus didelphys may be the presence of the vaginal septum. A division of the septum renders each cervix equally accessible to the admission of spermatozoa with subsequent pregnancy in either one or both uteri.

I wish to thank Dr. Isaac Diamond for referring the patient as well as for his active participation in the treatment and management of the case.

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CASE REPORT OF CONGENITAL ABSENCE OF LOWER HALF OF VAGINA AND HEMATOCOLPOS

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THE literature contains many articles regarding congenital absence of the entire vagina and the surgical repair of these cases,[2, 3] but congenital absence of the lower third of the vagina seems to be a rare deformity. Koff[1] states that "apparently, the upper two-thirds of the vagina never develops independently of the lower one-third." It has been fairly well established that the upper two-thirds of the vagina develops from the Müllerian ducts and the lower one-third of the vagina from the urogenital sinus.[4] In the case to be reported there was apparently a failure of development of the lower one-third of the vagina or possibly a failure of fusion of the upper and lower portions of the vagina. Few articles discussing the surgical repair of congenital absence of the lower part of the vagina were found in a review of the literature.[5] Therefore, it was felt important to report this case and the simple surgical repair that was used to correct this deformity.

Case Report

(Case No. 112101, UNH) A 17-year-old single nulliparous white girl entered the University Hospital on Oct. 14, 1952. She complained of productive cough, weakness, pain in the left upper quadrant, with recurring bouts of fever, chills, nausea, and vomiting at approximately three-month intervals. These symptoms had been present for approximately the last 6 years. The patient stated she had never menstruated. The past history consisted of the usual childhood diseases and the performance of an appendectomy in 1947. Examination in April, 1952, revealed hypothyroidism and chronic bronchitis. No pelvic examination was done at that time.

Physical Examination.—On admission the patient appeared to be about 12 years old instead of her stated age of 17. She was cooperative and cheerful, but seemed somewhat mentally retarded. The breasts were small and underdeveloped. The thyroid gland was without enlargement or palpable masses. On examination of the abdomen there was revealed an enlarged, smooth, nontender spleen approximately 3 fingerbreadths below the left costal margin. The liver also was enlarged to approximately 1 fingerbreadth below the right costal margin. There was scanty pubic hair of female distribution.

The labia were normal, although somewhat underdeveloped. The urethral meatus appeared normal. The vagina appeared to be absent except for a slight indentation approximately 0.5 cm. in depth just below the urethral meatus. No vaginal vault could be found. The rectoabdominal examination disclosed a 7 cm. soft, cystic mass, palpable high in the cul-de-sac in the midline. The uterus and adnexa could not be definitely outlined.

Laboratory Data.—On admission the hemoglobin was found to be 12.5 Gm., with 4.69 million red blood cells. The total white count 6,800, the differential count showing polymorphonuclear leukocytes 31, staff cells 42, eosinophils 1, lymphocytes 18, monocytes 8.

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Subsequent blood examinations consistently showed toxic granules in the neutrophils, slight hypochromia, and an elevated staff count. The urinalysis was negative except for an occasional trace of albumin. Bleeding, coagulation, and prothrombin times were normal. The basal metabolic rate was minus 18 on two occasions. The 17-ketosteroids in the 24 hour urine specimen amounted to 2.4 mg. The excretory urogram showed that the kidneys, ureters, and bladder were without abnormalities. Bone marrow studies showed granulocytic hyperplasia and hypercellularity. Papanicolaou smears from the indentation below the urethral meatus showed cytology compatible with that of the follicular phase.

Clinical Course.—The patient was suffering from chills and fever on admission on Oct. 16, 1952, and examination revealed nasopharyngitis, râles in the right lung field, and marked tenderness to palpation of the enlarged spleen, but with a few days of treatment with penicillin she became afebrile. A complete work-up on the Medical Service revealed that the patient had minimal bronchiectasis, hypothyroidism, congenital ichthyosis, and splenomegaly of undetermined etiology. With the findings of underdevelopment of the secondary sex characteristics, congenital absence of the vagina, and a pelvic mass, it was decided that an exploratory laparotomy should be performed to determine the exact status of the internal genitals.

Fig. 1.—Diagram to show anatomy of hematocolpos due to occlusion of the lower third of the vagina.

On Nov. 8, 1952, this exploratory laparotomy was done and an adolescent type of uterus, tubes, and ovaries was found. There was a 7 cm. cystic mass directly below the uterus displacing it upward. The diagnosis of hematocolpos was made (Fig. 1). The abdomen was closed and the patient was placed in the lithotomy position.

A small transverse incision approximately 4 cm. long was made just below the urethral meatus and above the fourchette. A space was then formed by blunt dissection between the bladder and rectum to a depth of approximately 8 cm. A finger in the rectum and a sound in the bladder aided in this dissection. The caudal wall of the cystic mass was then encountered. The cyst was opened and a large amount of "prune-juice-like" fluid was evacuated from the cyst cavity. The cavity was then washed with saline solution until clean. The cervix was identified at the top of the cyst cavity, and the uterine cavity was probed to a depth of 2 inches. The wall of the hematocolpos was then mobilized by blunt dissection for approximately 3 cm. about its opening and the edges of the opening were brought down and sutured to the skin about the perineal incision with interrupted chromic No. 00 sutures. This completely lined the tunnel made between the bladder and rectum with vaginal mucosa and formed a vagina approximately 4 inches deep. The newly formed vagina was packed tightly with gauze.

The pack was removed in 24 hours and a ¾ inch Lucite dilator, 3¾ inches long was inserted (Fig. 2). This dilator was made from a round Lucite rod. A hole was drilled through the center of the rod forming a lumen which allowed drainage while in place. Another hole was drilled transversely through one end of the rod. This allowed attachment of a string which facilitated removal. After one week the dilator was removed. The dilator was then inserted each evening upon retiring and removed in the morning and cleaned. Warm saline douches and Zepharin instillations were then started. After two weeks the patient was taught to insert the dilator herself. She was discharged four weeks postoperatively after healing of the vaginal mucosa was almost complete. She was instructed to continue the dilations twice daily and to return in one month to our gynecology clinic. She was placed on thyroid, 1 grain daily, and started on a 20 day course of Premarin, 1.25 mg. three times a day. Premarin was given to aid in the healing of the vaginal mucosa and also to test the response of the endometrium.

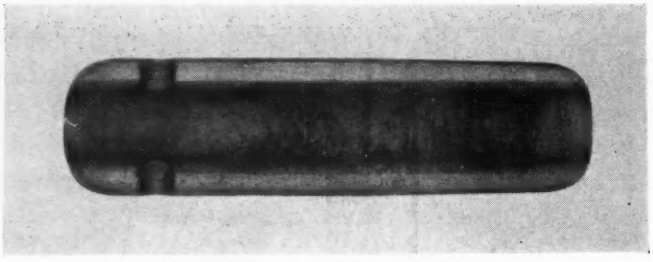

Fig. 2.—Lucite vaginal dilator.

Follow-up Visits.—The patient was again seen on Jan. 12, 1953, approximately 2 months after her operation. She stated that she had felt well since discharge, but had some difficulty inserting the dilator. She developed vaginal bleeding on January 11, five days after the completion of the 20 day course of Premarin.

Examination now revealed a vagina 4 inches deep and 2 fingerbreadths in diameter except for a narrow stenotic band 1 inch from the vaginal orifice. It was completely epithelized by healthy-appearing vaginal mucosa. The cervix was small, clean, and firm, with a slight amount of dark blood oozing from the cervical os. The uterus was anteflexed, symmetrical, firm, small, and mobile. No adnexal masses were palpable. Physical examination still revealed congenital ichthyosis, and splenomegaly.

The patient was readmitted to the hospital on January 15. She was taken to surgery where the stenotic band was incised anteriorly and closed transversely with interrupted No. 000 chromic sutures. A larger Lucite dilator, 1 by 3¾ inches, was inserted and kept in place for two days. The dilator was then removed, cleaned, and dilatations were carried out by the patient under the nurses' supervision twice daily throughout the rest of her hospital stay.

The patient was restudied by the Medical Department and no cause for the splenomegaly could be established, although blood and bone marrow studies still showed hypercellularity and increase in the immature forms of the granulocytic series. On dismissal, the vagina would admit 2 fingers with a depth of approximately 4 inches.

The patient was discharged January 19, on thyroid, 1 grain, and instructed to continue vaginal dilatations with the dilator once daily.

The patient was last seen on March 31, 1953. She had had a 5 day menstrual period March 13 to 18. The vagina was normal in depth and diameter with no areas of stenosis or inflammation. It was felt advisable to continue the dilatations and frequent check-ups for at least 6 months. Counseller[3] has pointed out the importance of dilatations to prevent postoperative stenosis in those patients who had to be operated on before marriage. One wonders what part absorption of menstrual blood from the hematocolpos could have played in the blood and reticuloendothelial-system changes seen in the patient.

Summary

1. A case of congenital absence of the lower half of the vagina with hematocolpos is presented.

2. The simple surgical technique used to correct this deformity is described.

3. The importance of careful follow-up and dilatations is stressed and a simple, effective dilator is described.

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UTERUS DIDELPHYS*

A Case Report

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BECAUSE of the numerous different classifications of uterine anomalies, it would probably be wise to start this report with a brief review of the various types of anomalies and to define what we mean by the term uterus didelphys. It seems, in a review of the literature, that many of the authors have elaborated upon, or simplified classifications used previously to the articles they have written. Litzenberg,[13] in his *Synopsis of Obstetrics,* lists six different types of anomalies; Stander,[18] in *Williams Obstetrics,* 14; and Greenhill,[6] in his latest edition shows 11. One of the simplest classifications is that of Jarcho.[11]. It is as follows: (1) uterus didelphys, (2) uterus duplex, (3) uterus bicornis, (4) uterus septus, (5) uterus subseptus, (6) uterus arcuatus, or cordiformis, and (7) uterus unicornis.

The case under discussion is one of uterus didelphys with duplications of cervix and vagina. The cause of these anomalies is generally believed to be related to the embryological development of the Müllerian ducts, and due to either failure of fusion of the ducts as in the case of uterus didelphys, persistence of the wall median to the ducts, as in uterus septus, or failure of development of one of the ducts, as in uterus unicornis. Obviously there are all degrees of development and combination of the three processes just mentioned above to be found.

The incidence of uterus didelphys is not known. It is considered to be a comparatively rare anomaly. The reason it is difficult to arrive at a definite incidence is the difficulty in diagnosis. The condition is, of course, quite compatible with life, and in many cases it is not discovered until postmortem examination, or until some other pathological condition calls attention to it. Uterus didelphys is most commonly found during pregnancy, though there are some cases published in which the malformation was not noted until the second or third child was born. The patient under discussion was unaware of the malformation, although she had had two previous pelvic examinations elsewhere in the preceding 12 months. Jarcho[11] notes, in review of the records of the New York Lying-In Hospital, that in a 25 year period there were 114,243 consecutive obstetrical admissions, and in these there were only 4 cases of uterus didelphys. In a subsequent 5 year study at the same hospital, there was one case of uterus didelphys in 27,703 obstetrical admissions. Fenton,[5] in a review of the records of the Sloane Hospital for Women, for

*Presented at a meeting of the Minnesota Obstetrical and Gynecological Society, Minneapolis, Minn., Dec. 6, 1952.

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the years 1933 to 1942, and encompassing 60,768 deliveries, found 29 cases of uterus didelphys. A review of the literature indicates that there are approximately 400 published cases of uterus didelphys. It has been theorized that superfetation can occur in patients with uterus didelphys. Twin pregnancy is also more common in patients with double uteri. One group of authors state that the incidence is one in twelve pregnancies, instead of the usual one in eighty-nine anticipated in patients with a normal, single uterus. Uterus didelphys is of little significance other than its interest as a medical curiosity, except when pregnancy occurs; then it must be considered a complication of pregnancy. Occasionally, in the nonpregnant individual, it may cause dysmenorrhea, dyspareunia, or even sterility, and any one of these complaints may lead to a diagnosis of uterine anomalies. Most patients with uterus didelphys are able to conceive easily, unless there is some developmental mechanical barrier. Some authors state that these patients have an increased fertility index. The abortion rate is definitely increased. This is probably due to one of several factors, such as abnormal implantation, poor vascularization, fundic irregularities, or malposition of the gravid uterus.

In the pregnant patient at term, the mode of delivery must be decided upon. Reports in the literature are about equally divided between those that favor section, and those that elect vaginal delivery. We believe that this is an individual matter, and has to be based on the individual patient. Quite often patients with uterus didelphys will have abnormal presentations, but many will go through labor and deliver normally. One must be aware of the prolonged difficult labors. As we have already noted, the muscular development of the uterus is sometimes inadequate and this can lead to inert labor, and theoretically to uterine rupture, though we have not found any cases of rupture in our brief review of the literature. A long rigid cervix, especially since it is usually attached to the other uterus at this point, can cause obstruction to labor, and often a nonpregnant uterus will rotate posteriorly and become incarcerated in the pelvis, causing mechanical obstruction. In our particular case, section was decided upon because of the breech presentation in a primigravida, and the fact that the nonpregnant uterus could be felt in the pelvis, posterior to the pregnant uterus, and in this position obstruction in labor was feared. The third stage of labor can also be dangerous in the patient with uterus didelphys. The incidence of hemorrhage is greater than in patients with normal uteri. Again, this is probably due to the poor muscle tone and the position of the attachment of the nonpregnant uterus. Retained placentas are also common. Most authors agree that plastic surgery beyond the removal of the vaginal septum in these individuals is not a wise procedure, and does not increase the chances of normal delivery.

Case History

Mrs. G. J., an 18-year-old para 0, was first seen on March 29, 1950. At that time she complained of amenorrhea since Jan. 21, 1950, nausea, and vomiting, mastalgia, and urinary frequency. Her past history was essentially negative. The menarche had occurred at age 13, and the menses had always been somewhat irregular, lasting 3 to 4 days, with

moderate bleeding. There was no history of dysmenorrhea. General physical examination revealed a well-nourished, well-developed, white woman of asthenic build, in a good state of health. Pelvic examination revealed an early intrauterine gestation. No other significant observations were recorded at this time. Laboratory data were as follows: Serologic tests negative, Rh factor positive, hemoglobin 12.4 Gm. or 87 per cent, white blood count 12,600, red blood count 4.24 million, urinalysis negative.

The patient was instructed to return in 3 weeks. Detailed pelvic examination at this time revealed the presence of double vaginas, double cervices, and the existence of a double uterus was suspected. The two vaginas were marital, both admitting two fingers with ease, the right being slightly larger in diameter. They were separated by a rugous septum (0.5 cm. in diameter), which extended from a point 1 cm. within the hymenal ring to the cervices. This septum completely resembled the lateral vaginal walls in appearance and in elasticity. The cervices were nulliparous, and presented normal portios, both endocervical canals appearing patent. The right cervix was somewhat larger and presented a positive Goodell's sign. The left cervix was more firm and red. The uterus was enlarged to the size of 12 to 14 weeks' gestation, soft, and lay predominately in the right side of the pelvis; it appeared to be attached to both cervices; a suggestive mass of smaller size was felt in the left side of the pelvis. Pelvic measurements were as follows: Spines 24, crests 27, external conjugate 19, diagonal conjugate 11.5 plus, true conjugate 10.5 plus. The pelvis was typed as adequate, gynecoid.

Fig. 1.—Anteroposterior hysterosalpingogram showing double uterus.

The prenatal course was entirely uneventful. The patient was seen on 13 occasions from March 29, 1950, to Oct. 11, 1950. The blood pressure determinations were between 100/60 and 130/80. Urinalyses were consistently negative. Her total weight gain was 16 pounds. Pelvic examination on May 31, 1950, definitely confirmed the suspicion of uterus didelphys, the pregnancy being in the right uterus. Breech presentation was diagnosed clinically on Aug. 23, 1950. The fetus remained in this position until term. Roentgenogram on Sept. 20, 1950, confirmed the fetal position. After considerable deliberation an elective cesarean section was decided upon as the method of delivery because the non-

pregnant uterus had shifted to occupy the entire pelvic cavity, lying posterior to the lower segment of the pregnant uterus. This presented the problem of soft tissue dystocia with breech presentation.

Accordingly, on Oct. 18, 1950, the patient was brought to surgery and an elective low corporal cesarean section was performed under low spinal anesthesia. This type of procedure was elected in preference to the low segment method of approach because of the peculiar anatomic condition encountered in this particular patient. Examination of the pelvic contents revealed a uterus of term size, occupying the right side of the abdomen, containing a fetus in the right sacroanterior position. Attached to the right cornual portion of this organ were a normal tube and ovary. The left uterus had undergone sympathetic enlargement; it was the size of a three months' gestation, was attached rather loosely to the left lateral portion of the right cervix, and had undergone torsion, so that it completely filled the true pelvis, having rotated posteriorly to the pregnant uterus. A single tube and ovary were attached to the left cornual portion of this uterus.

A viable term male infant who weighed 5 pounds, 15½ ounces was delivered without incident. The placenta was manually extracted and the remainder of the surgical procedure completed in routine fashion.

The postpartum course was uneventful and the patient was discharged on the eighth postpartum day.

Pelvic examination six weeks after delivery revealed involution progressing in normal fashion. There was minimal bleeding from the right external os; the left was clean. Both canals were sounded with ease. The right uterus was enlarged 1½ times and moderately firm, anterior in position. The left uterus was of normal size, position, and consistency. The remainder of the pelvic and abdominal examination was within normal limits.

The patient returned one month later and hysterosalpingography was done (Fig. 1).

Final examination on Feb. 16, 1951, was essentially negative and pelvic findings were as above.

Conclusion

A case of uterus didelphys with double vagina, and its management during pregnancy is presented.

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A CASE OF POLIOMYELITIS COMPLICATING PREGNANCY WITH DEATH OF MOTHER AND BABY

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THE mortality from poliomyelitis is higher in the pregnant than in the nonpregnant group. Bowers and Danforth,[1] after reviewing the literature and adding 24 new cases of their own, found that the death rate in 428 cases of poliomyelitis complicating pregnancy was 9.7 per cent. The over-all seven-year mortality rate in their hospital was 6.25 per cent. These authors also found that the most dangerous time for a pregnant patient with acute poliomyelitis was the period immediately following delivery. They state: ". . . 12 per cent of the maternal deaths occurred in this small group which comprised only 3.5 per cent of the total cases of poliomyelitis associated with pregnancy." The actual mortality in this group was 33.3 per cent. The following case underlines this statement and in addition presents several interesting features.

A 31-year-old para iii, gravida iv, entered the hospital on Dec. 27, 1952, with painless vaginal spotting of a few hours' duration. Her last menstrual period had been on April 2, 1952, and the estimated date of confinement was Jan. 9, 1953. Her three previous pregnancies had been entirely normal. Her family and past histories were noncontributory. The current pregnancy, except for a 30 pound weight gain, had been normal until the day before admission. That evening she developed a backache which became quite severe and prevented her from sleeping. This was still present on admission, and was very troublesome for twenty-four hours, but quieted down after bed boards were put under the mattress. She complained of being tired and feeling weak which was not surprising in view of the very strenuous life she had been leading the few days previously. She also had a moderate degree of sinusitis, though her temperature was normal at all times. She was very apprehensive and felt she had poliomyelitis, having had a contact a month earlier. A neurological check at that time showed no abnormalities. The bleeding stopped shortly after her arrival at the hospital.

The day after admission, December 28, the membranes ruptured spontaneously but she did not go into labor. She still complained of feeling tired, and of a headache which was interpreted as being due to the sinusitis. Her temperature remained normal and she had no neurological symptoms. At 3:00 A.M., on December 29, she felt a few uterine contractions but they did not last. While they were going on she had to be catheterized once, but at all other times while in the hospital she voided spontaneously. On the afternoon of December 29, as she had not started in labor, an intravenous infusion of 1,000 c.c. of 5 per cent glucose and 5 minims of Pitocin was begun and labor started two hours later. The head was high and labor was slow due to a posterior occiput. Eventually around 10:30 P.M. the cervix was fully dilated with the head at the ischial spines and still posterior. In view of the fact that she was very tired, having had no sleep for two days, she was delivered from this position by a moderately easy Scanzoni maneuver. The baby was a 7 pound, 3½ ounce male that breathed spontaneously and appeared normal. The third stage of labor was entirely uneventful. The

patient was given 0.2 mg. of Ergotrate intravenously after delivery of the baby. The placenta and membranes were intact. The uterus remained firm and the patient lost a minimum of blood. For two hours before delivery she was given nitrous oxide and oxygen with the pains and one hour before delivery she was given 1/200 grain scopolamine. The delivery itself was done under spinal anesthesia, 5 mg. of Pontocaine given in the third lumbar interspace. This combination was used because of the sinusitis.

During the night, after the delivery, she was somewhat irrational and tried to get out of bed, but by morning her sensorium was entirely normal. All during the day of December 30, she complained of difficulty in breathing and examination of the chest showed typical asthmatic squeaks and groans. She had never had asthma but did have hay fever and one of her children had asthma. She continued to be apprehensive and restless but at no time was she febrile. In the afternoon a medical consultant was called. He confirmed the diagnosis of asthma, and made a complete neurological examination which was normal. He instituted treatment for the asthma consisting of an intravenous infusion containing aminophylline, ephedrine, and phenobarbital, and by midnight she was much better. She was seen several times by the resident during the early morning and the improvement continued. When he last saw her at 5:00 A.M. she was comfortable, breathing easily, and for the first time was not apprehensive. At 7:15 A.M. she was found to be in poor condition, with poor color and labored breathing. Before oxygen could be started she died.

An autopsy was obtained which showed mild acute suppurative bronchitis and acute anterior poliomyelitis, bulbar type. There was no myocarditis.

The baby did very well until the morning of January 6. That day he appeared lethargic and had a poor sucking reflex. He was immediately transferred to the Children's Medical Center. Paralysis was progressive and severe. He died several days later of poliomyelitis, bulbar and spinal type.

Comment

It is regrettable that the diagnosis of poliomyelitis was made only at autopsy in this case. This is in spite of the fact that it was seriously considered in the differential diagnosis during her hospital stay. The backache and headache were the only signs present. The former improved with orthopedic treatment, the latter was attributed to her sinusitis. The difficulty in breathing was thought to be due to asthma and improved on antiasthmatic treatment. She did have to be catheterized once, but this coincided with rupture of the membranes.

After the diagnosis had been made, further questioning of the husband brought out the fact that on the night of December 26, the backache had not responded to codeine, dose unknown. Also he had noted a transitory episode of dysphagia about three hours after delivery. This was not noted by anyone else and when the medical consultant examined her later on she was able to drink and swallow without difficulty. At no time was there paralysis or demonstrable muscle weakness and she remained afebrile throughout her course.

At autopsy the age of the lesion was estimated at about seven days. This would mean that the infection began on December 23 or 24. During those days and until admission to the hopsital the patient was extremely active and busy, doing a great deal of work and getting relatively little sleep. Since undue physical activity in the acute stages of poliomyelitis increases the risk of paralysis,[2] this is perhaps significant.

This patient died in the immediate postpartum period. It is this period that is described by Bowers and Danforth[1] as being the most dangerous for

a pregnant woman with poliomyelitis. It might be more accurate to say that the danger lies in a patient delivering during the phase of the acute infection. The authors just cited give the maternal mortality from poliomyelitis in the first six months as 6.5 per cent. This is very close to their over-all mortality from the disease of 6.25 per cent and would indicate that pregnancy has little if any effect on the disease in these early months. The maternal mortality jumps to 15.1 per cent in the third trimester. This is largely a reflection of the mechanical difficulties which the uterus near term imposes on the patient's breathing. However, if the patient delivers while she has the acute infection, as did the patient here reported, the mortality rises to something approaching one in three. These observations would suggest that every effort should be made to prevent the onset of labor during the acute phase unless the size of the uterus causes respiratory embarrassment. They would also suggest that while the supply of gamma globulin is limited, it should be used only in the last month of pregnancy since the immunity it induces lasts only about five weeks.[3]

The fate of the baby in this case is unusual. Writing in 1951, Shelokov and Weinstein[4] pointed out that there were only about 150 known cases of acute poliomyelitis in infants under 6 months and that all but 3 of these were over 2 weeks old. This baby had no contact with his mother after birth. Since the minimum incubation period is generally accepted as 7 days, this probably represents an infection during delivery. This is likely, as the membranes were ruptured for thirty hours before delivery.

Complete studies of the baby and of the epidemic of which this patient's death was the one fatality were made by Dr. Sidney Kibrick of the Children's Medical Center, Boston, and will be reported in the literature at a later date.

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MIGRATION OF FOREIGN BODY FOLLOWING CRIMINAL ABORTION

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THE purpose of this report is to call attention to the value of x-ray in the diagnosis of all cases of suspected criminal abortion and the migration of foreign bodies without perforation of pelvic viscera. Review of the literature reveals numerous cases of migration of foreign bodies,[1] but none was found[2] in which a foreign body traversed the entire uterine cavity and internal and external tubal os without perforation. Elden[3] reports a case in which x-ray revealed the presence of a catheter in the pelvis following perforation of the uterus. Bateman[4] also reported a case in which abortion was attempted with a rubber catheter which was subsequently found in the abdominal cavity; Weisberg[5] and Frech[6] report other cases in which x-rays revealed the presence of a rubber catheter within the abdominal cavity following criminal abortion. These, and other similar case reports, show that onset of symptoms following abortion was short and the symptoms rather severe, indicating perforation of the uterus. This case report shows only mild symptoms with a rather long interval between the time of criminal intervention and the correct diagnosis and final operation.

The fact that x-rays would have made an earlier diagnosis and that a No. 16 French rubber catheter can pass from the cervical os into the abdominal cavity without perforation of the uterus or Fallopian tube is stressed.

Mrs. H. P. was a white woman, aged 35 years, married 13 years with one daughter 8 years of age. This patient was first seen on June 5, 1949, at which time a diagnosis of pregnancy of six weeks' duration was made. The patient did not seem unhappy to be pregnant, and was not seen again until July 2, 1949, at which time I was called to her home to see her because of vaginal bleeding and chills and fever. She was remorseful and tearful over having had a criminal abortion performed and stated that the abortionist "packed the womb" and told her to remove the pack in 48 hours. She had been unable to locate the pack and said that she thought it had come out while she was on the commode. She was taken to the office and a speculum examination revealed only the presence of blood exuding from the cervical os. She was given penicillin and made an apparent recovery in about a week. Three weeks later, the patient returned to the office complaining of mild pain in the pelvis, relieved by heat and aspirin. Pelvic examination was entirely negative and the patient was thought to have psychosomatic symptoms as a result of criminal abortion. The patient continued to return for treatment, was afebrile, and continued her housework. Several consultations were obtained and no evidence of pathology could be found. She requested operation on numerous occasions, but was reassured that no pathologic condition was present. The pain became gradually more severe, but not enough for patient to cease working. She again reported to the office on July 12, 1950, over a year following the criminal abortion, and examination at this time revealed a small tender mass in the right lower quadrant. She was sent to the hospital

and laparotomy was performed on July 17, 1950, under general anesthesia. The omentum was found to be adherent to the fimbriated end of the right tube, and a hard object protruded from the tube. This was traced the length of the tube and found to extend into the uterine cavity. The omentum was freed, and the large end of a No. 16 French rubber catheter was pulled from the uterus and tube (Fig. 1). The abdomen was closed and the patient had an uneventful postoperative course. She has remained free of symptoms since the operation.

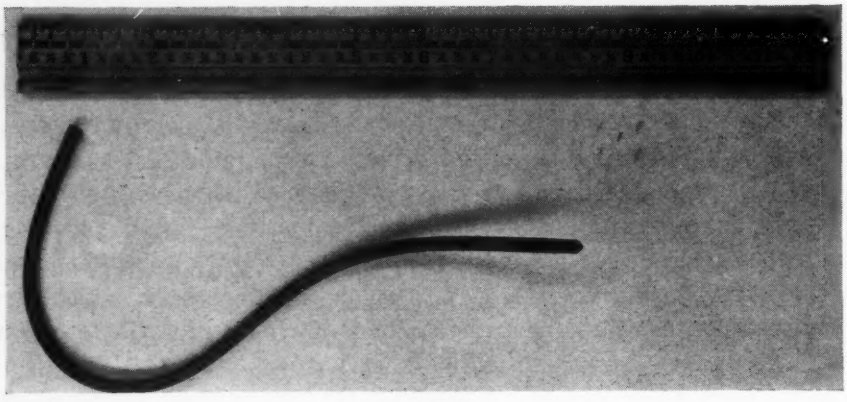

Fig. 1.

Summary

A case has been reported of the migration of a rubber catheter from the cervix through the uterus and tube without perforation of either. Failure to utilize x-ray resulted in persistence of symptoms for one year.

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PRIMARY CARCINOMA OF THE BARTHOLIN GLAND WITH FIVE-YEAR SURVIVAL

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PRIMARY carcinoma of the Bartholin gland is considered to be a rare type of vulvar malignancy. Wharton and Everett,[1] in a recent review of the literature report finding 104 cases and add 5 of their own. Pattison and Schute[2] reported another case in 1951. Of the total, 52, or 47.3 per cent have been adenocarcinomas, 39, or 35.4 per cent, have been squamous-cell carcinomas, and 19, or 17.3 per cent, included 4 sarcomas, 11 difficult to classify, and 4 unknown types.

The infrequency of the tumor accounts for the confusion in early diagnosis, the varied methods of treatment, and the meager information available regarding the course of the disease both with and without treatment. In the preulcerative stage the small firm nodule may be mistaken for a cyst, fibroma, chronic inflammatory process, or other benign condition. In the ulcerative stage differentiation from the more common vulvar malignancies is difficult. To be classified as a primary carcinoma of the Bartholin gland the tumor should fulfill Honan's[3] criteria. Of the many methods of treatment, that recommended by Taussig[4] is most generally followed today. This consists of a vulvectomy followed either immediately or at a second stage by a bilateral inguinal and femoral lymphadenectomy of the Bassett type. There has been some difference of opinion as to whether this vulvectomy should be partial or complete. Radium and x-ray formerly were used as a main effort but recently they have been used mainly following surgery, if at all. The prognosis has been uniformly poor. In only a small number of cases has there been any adequate follow-up study. Of the 110 cases in the literature only 9 patients who have survived five years without residual tumor are reported, of whom two have been followed for seven years and are free of malignancy.

The following case is presented as a primary carcinoma of the Bartholin gland treated surgically with a successful five-year subsequent course.

Mrs. E. A., a 55-year-old white married woman, was admitted to the Nazareth Hospital on Dec. 10, 1947, complaining of a lump in the left vulvar region and dyspareunia. She first noticed the lump one month previously. There was some uncertainty as to whether or not it had increased in size since the time it was first noticed. No history of previous swelling in the area, painful or otherwise, could be elicited.

The past history was significant in that thirty-two years previously a bilateral salpingo-oophorectomy was done for "inflammation of the pelvis." Details of this procedure were unobtainable. Her mother died of "cancer of the uterus."

On physical examination the only abnormal findings were limited to the pelvis. A slightly raised area was noted in the left vulva. Beneath the skin surface there was palpable a firm, stony hard, more or less movable mass about 2 cm. in diameter. Its location was in the area of the Bartholin gland. The tumor was only slightly tender.

The opposite vulva was normal. A small rectocele was present. The uterus was quite small but otherwise normal. Adnexal areas presented no unusual finding. Several small soft nodes were palpable in both inguinal regions. A small right inguinal hernia was present. Nothing of significance was revealed in the laboratory studies. A presumptive diagnosis of primary carcinoma of the left Bartholin gland was made.

Fig. 1.

Fig. 2.

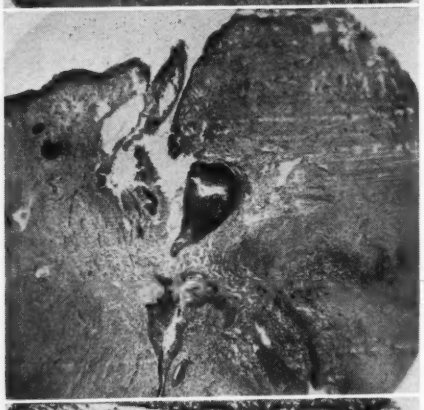

Fig. 3.

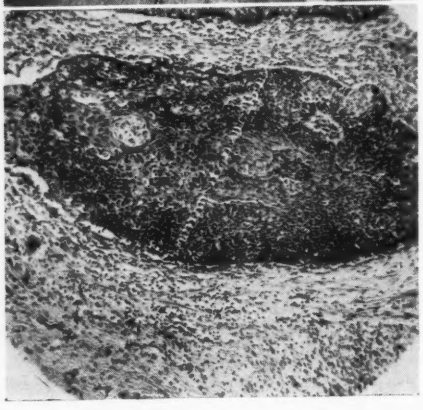

Fig. 1.—Section showing normal duct of Bartholin gland. (×25. Reduced one-third.)
Fig. 2.—Section through tumor area. (×25. Reduced one-third.)
Fig. 3.—Epithelial pearl formation. (×100. Reduced one-third.)

At operation on Dec. 13, 1947, it was decided to precede definitive treatment with a frozen section biopsy. The report being epidermoid carcinoma, a complete vulvectomy was done. On the left side the dissection was extended to the periosteum over the pubic ramus and well into the ischiorectal fossa. About half of the vaginal wall was removed on the left side. The postoperative course was uncomplicated. On Dec. 30, 1947, the

second stage was done. This consisted of a bilateral inguinal and femoral lymph node excision, both superficial and deep chains. Though many nodes were removed none had any gross characteristics of malignancy. A small right inguinal hernia of the direct type was repaired during the latter operation. Except for small areas of slough along the inguinal incisions the postoperative course was satisfactory.

Pathological Report.—Gross Examination: The specimen consisted of a ridge of tissue comprising the vulva with the labia majora and minora, clitoris, and fourchette. There was an elliptical piece of skin attached from above the clitoris to below the left inferior portion of the vulva. This extended for a distance of 5 cm. A portion of the above-described tissue was apparently a portion of the vagina on the left side. A duct was visualized in the vestibule. It could be entered a short distance whereupon an obstruction was met. Beneath and adjacent to this was a hard, indurated, fixed mass of tissue approximately 2.1 cm. in diameter. It cut with increased resistance, revealing a white, firm, granular surface which had surrounding tissue contracted toward it.

Microscopic Examination: Sections through the tumor revealed it to be composed of large irregular masses of cells. The individual cells were relatively large and had irregular nuclei which were hyperchromatic and in which numerous mitotic figures could be seen. In some places the tissue showed extreme undifferentiation while in others there was a tendency toward keratinization and epithelial pearl formation. In the centers of some of the aggregations of cells there was a nondescript necrosis and surrounding the groups of cells there was definite dense stroma formation. Close examination of the epithelial surface apparently showed an invagination of overlying squamous epithelium of the type seen in the vagina. This dipped down into a small recess at the bottom of which one might see cuboidal epithelium of the type one sees in ducts. There had been almost complete destruction of the Bartholin gland and its normal architecture, a neoplastic epithelial process replacing it.

Diagnosis.—Epidermoid carcinoma of the Bartholin gland, squamous cell, Grade II.

Microscopic study of the many lymph nodes revealed only lymphoid hyperplasia and fibrosis with no evidence of malignancy in any of the nodes.

Follow-up Course.—The patient has been seen at six-month intervals for five years. During the first six-month period there was a small area of lymphedema at the former left saphenofemoral junction. This gradually disappeared. About two years after operation a small cystocele and rectocele were present. It appeared probable that poor support on the left vaginal wall as a result of operation may have contributed to the development of these. Repair was performed immediately and there has been no recurrence to date. No evidence of recurrent malignancy has been found.

Comment

The paucity of cases of primary carcinoma of the Bartholin gland and the almost complete lack of adequate follow-up observations of those treated make it difficult to draw any general conclusions regarding the proper management of a particular case. It has been suggested that if the tumor is small and probably still within the gland capsule a conservative operation might be sufficient. It is also believed that the rate of metastasis is slow. Vulvectomy with radical lymph node dissection was chosen in the case herein reported as being the procedure offering the best hope of permanent arrest of the malignancy. No radiation therapy was used either before or after surgery.

To the nine previously reported five-year survivals is added a tenth case.

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INFECTIOUS MONONUCLEOSIS

Report of a Case* With a Localized Tumor (Simulating Cancer) in the Cervix Uteri

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THE manifestations of infectious mononucleosis are protean. The onset is similar to that of many acute infectious diseases, with vague constitutional complaints in the first four or five days. The presenting signs are extremely variable and may simulate such conditions as follicular tonsillitis, Vincent's angina, German measles, infectious hepatitis, appendicitis, meningitis, agranulocytosis, acute leukemia, purpura hemorrhagica. In his monograph on infectious mononucleosis, Glansmann[1] mentioned the occasional occurrence of leukorrhea in adolescent girls suffering from this disease. However, a review of the hematologic literature from 1932 to 1951[2] failed to disclose any cases in which the presenting symptoms or signs suggested a carcinoma of the cervix uteri. It is the purpose of this presentation to report such a case.

Mrs. N. K. L., white housewife, aged 25 years, entered the University of California Hospital on Oct. 3, 1946, for diagnosis and treatment. Approximately three weeks before admission to the hospital she first noted a moderate, thin, yellowish vaginal discharge. At about the same time she had a sore throat, bleeding gums, coryza, and generalized malaise. She had no cough, pleuritis, or hemoptysis. She consulted her family physician who treated her with sulfadiazine and penicillin, without benefit.

One week later, an expected menstrual period occurred. It was normal in all respects until the fourth day, when the flow was replaced by a fairly profuse clear, thin, yellowish discharge. This was accompanied by an elevation in temperature to 103-104° F. Because of the vaginal discharge, the patient was referred to a gynecologist, who discovered a sloughing, fungating lesion involving the entire visible portion of the cervix and extending about an inch into the uterine canal. A biopsy was performed, and a diagnosis of "extremely anaplastic carcinoma" was made. The patient was then referred to the University of California Hospital for definitive therapy.

The history revealed that her husband had had a sore throat, coryza, generalized malaise, and low-grade fever prior to the onset of the patient's illness. His symptoms were not severe enough to keep him from work or to prompt him to seek medical advice.

Physical examination disclosed a well-developed, well-nourished woman, who complained of "a feverish feeling" and malaise. She was apprehensive because a grave prognosis had been given. The skin was normal. The lymph nodes in the cervical, axillary, and inguinal regions were discretely enlarged and nontender. The ears, eyes, nose, and throat were normal, apart from a small ulcer on the left posterior tonsillar pillar. The heart and lungs were normal. A smooth, moderately tender liver edge was palpable two fingerbreadths below the right costal margin. A slightly tender spleen was palpable three fingerbreadths below the left costal margin.

*We wish to thank Dr. S. P. Lucia for permission to report this case.

On pelvic examination, the cervix felt rather soft and bulbous. The uterus was anterior in position, not enlarged, freely movable. There was no parametrial induration. On inspection, the cervix appeared irregular and necrotic. A polypoid mass was seen extending from the uterine canal.

The remainder of the physical examination showed no abnormalities.

Serologic tests for syphilis were negative. The blood examinations revealed 12.8 Gm. of hemoglobin per 100 ml. of blood, an erythrocyte count of 4.48 million and a leukocyte count of 5,950 cells per cubic millimeter. The differential count revealed 23 per cent segmented neutrophils, 4 per cent neutrophilic band cells, 1 per cent basophils, 2 per cent monocytes, and *70 per cent lymphocytes.* The majority of the lymphocytes were fenestrated and monocytoid in appearance. The Paul-Bunnell heterophil antibody test was positive on two occasions with titers as high as 1 to 1,792. A clinical diagnosis of infectious mononucleosis was established.

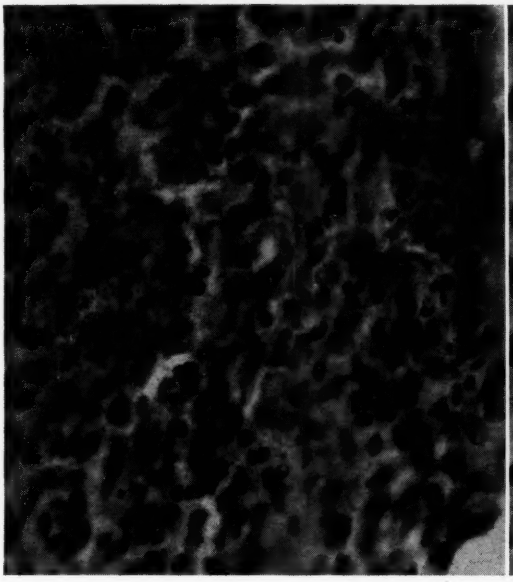

Fig. 1.

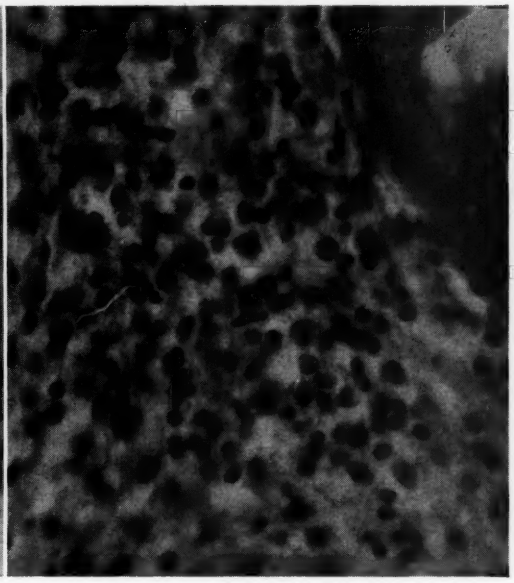

Fig. 2.

Fig. 1.—First biopsy of cervical mass. Diagnosis: anaplastic carcinoma.
Fig. 2.—Second biopsy of cervical mass. Diagnosis: subsiding inflammatory reaction.

The patient was reassured and treated symptomatically. A second biopsy of the cervical lesion was performed 13 days after the first one, and the diagnosis was "subsiding inflammatory reaction."

The patient recovered uneventfully and an examination of the genital tract six months later showed no abnormalities.

Comment

Sore throat is perhaps the most common presenting symptom of infectious mononucleosis. It is astonishing that vaginitis and endocervicitis have not been reported as chief complaints in this condition, since the anatomic distribution of lymphatic tissue in relation to mucous membrane in the female pelvis is similar to that in the oropharynx. The fact that a pelvic examination may not be done when the diagnosis is established may be responsible for the failure to discover the vaginitis and/or endocervicitis in infectious mononucleosis.

This case history illustrates the importance of a careful examination of the blood as an integral part of the physical examination. The diagnosis of infectious mononucleosis could have been established and the relationship of the vaginal lesion to the disease could have been suspected if a careful routine blood count had been performed. In addition, the patient could have been spared the mental anguish.

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ENDOMETRIAL OSSIFICATION

Report of Two Cases

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GENERALIZED calcification and osseous metaplasia of endometrium are medical curiosities. Their rarity and an interest in the metabolic conditions leading to these changes have prompted a report of two cases observed at the Pathology Laboratory of the New England Deaconess Hospital.

Case 1.—(149153) C. L., a 36-year-old white woman, was first seen in August, 1942, with symptoms of hyperthyroidism of 10 months' duration. She had lost 30 pounds in weight, and her pulse was 110 and blood pressure 180/100. The basal metabolic rate was plus 83.

In 1936, at the age of 19, this patient had aborted at 6 months. Three years later she delivered viable term twins, but during the last trimester she had elevated blood pressure and marked ankle edema. The following year she was again pregnant, and, although she had elevated blood pressure and convulsions during the last 2 months, she delivered a viable term fetus.

On Aug. 20, 1942, after 10 days' treatment with Lugol's solution, a bilateral subtotal thyroidectomy was performed. Pathological diagnosis (No. 63714) was primary hyperthyroidism with moderate involution and slight strumitis. She remained free of symptoms and repeated basal metabolic rate determinations were within normal limits until August, 1945, when she complained of nervousness, palpitation, and heat intolerance. The basal metabolic rate was plus 18, and an enlarged thyroid remnant could be felt on the left side of the trachea.

She was next seen in October, 1948, when her symptoms became more pronounced. Her BMR was found to be plus 38. She was begun on Lugol's solution, 10 drops daily. She was followed at frequent intervals, and on Aug. 9, 1949, in addition to the iodine, she was started on propylthiouracil, 300 mg. daily. On Sept. 21, 1949, the thyroid remnants were removed. The left remnant weighed 10 grams and the right weighed 5 grams. Pathological report (No. 117378) was recurrent primary hyperthyroidism with moderate involution and strumitis.

The patient developed marked laryngeal edema with bilateral cord paralysis, and the following day a tracheotomy was performed. The edema rapidly subsided and the tracheotomy tube was removed. There was return of cord function prior to the patient's discharge on the seventh postoperative day.

On September 23 (48 hours after operation), serum calcium was 8.0 mg. per cent, and on September 27 the level was 8.2 mg. per cent. The parathyroid glands were not seen on the resected remnants, and the patient displayed no evidence of tetany during her week of postoperative hospital stay. However, shortly after returning to her home in a neighboring state, she had to be hospitalized for treatment of tetany, characterized by marked carpopedal spasm and great difficulty in breathing. Following her return from the hospital, she took oral calcium for 2 weeks, and in addition was given intravenous calcium on 4 occasions.

She was next seen on Nov. 23, 1949, at which time she was found to have carpopedal spasm and positive Chvostek and negative Trousseau signs. The calcium level was 6.4 mg. per cent. She was begun on calcium lactate, 2 drams 3 times daily, and vitamin D, 50,000 units twice daily. On Dec. 27, 1949, the calcium level was 9.2 mg. per cent and BMR plus 9. Pulse was 72 and weight 145 pounds.

On July 13, 1950, the patient was free of symptoms, the serum calcium was 9.4 mg. per cent and serum phosphorus was 2.7 mg. per cent. The calcium was decreased to 1 dram daily and the vitamin D was continued at 50,000 units daily. She continued this medica-

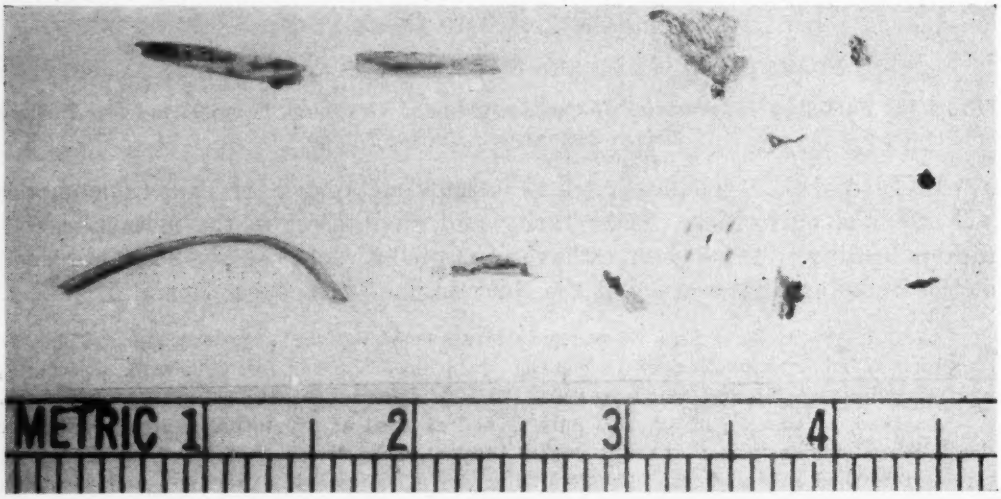

Fig. 1 (Case 1).—Demonstration of the gross resemblance of ossified endometrium to fetal bones.

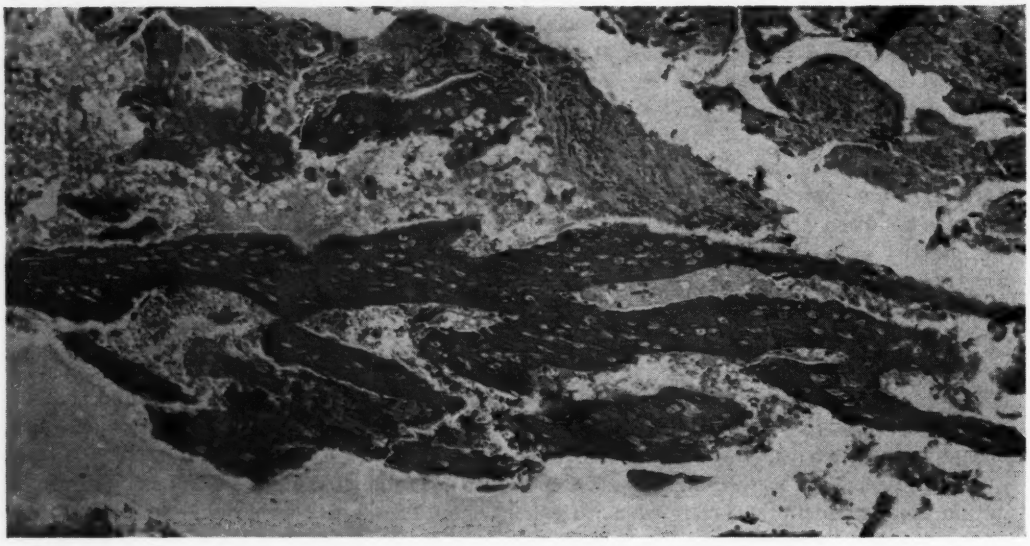

Fig. 2 (Case 1).—Ossification of endometrial stroma. Scattered endometrial glands remain. (Hematoxylin and eosin. ×125. Reduced one-fifth.)

tion for 2 months, then stopped all medication for a month. At the end of this trial period, she had return of her breathing difficulty and hand tingling, and the serum calcium had fallen to 7.6 mg. per cent with a rise of serum phosphorus to 4.6 mg. Calcium lactate and vitamin D were resumed, with doses of 2 drams and 50,000 units daily, respectively.

In October, 1951, she was found to be two months pregnant. Her blood pressure was 190/130, and termination of the pregnancy was advised. She had no evidence of hyperthyroidism, and the BMR was plus 3. She was taking 20 grains of calcium daily, but had

taken no vitamin D for the preceding month. Serum calcium was 8.0 mg. per cent. She was advised to increase the calcium to 2 drams daily and to resume the vitamin D. A therapeutic abortion was performed elsewhere in October, 1951.

She was seen again on July 30, 1952, at which time she complained of tingling of tongue and lips and stiffness of the hands. She also had frequent attacks of "faintness" and a "numb" sensation in the chest and face. There was a positive Trousseau sign, and serum calcium was 8.2 mg. per cent.

For the 9 months following the therapeutic abortion, she had had almost constant vaginal bleeding with increase in bleeding at the time of expected menses. A dilatation and curettage and biopsy of the cervix were done on July 31, with recovery of a small amount of soft gray-red tissue and several pieces of calcified material resembling fetal bone. These latter were about 1 cm. long and 0.1 cm. thick, and one piece was flat and triangular, measuring 0.4 cm. in greatest diameter (Fig. 1).

Microscopically, the endometrial stroma was largely replaced by an irregular network of bony trabeculae. Osteocytes were present but no osteoblasts or osteoclasts (Fig. 2). Glands identified were in the proliferative phase. There was no evidence of pregnancy.

Diagnoses of chronic endocervicitis and endometrium with marked metaplastic ossification of stroma, suggesting hypervitaminosis D, were made.

Fig. 3 (Case 2).—Bony trabeculae in the endometrial stroma. (Hematoxylin and eosin. ×125. Reduced one-fifth.)

CASE 2.—(90773) N. M. U., a 34-year-old married woman, at the age of 15 years, had acute rheumatic fever with polyarticular rheumatism, and required hospitalization for one year. An acute recurrence at age 23 again required 2 months of hospitalization.

At age 31, she had a therapeutic abortion at 3 months because of decompensated rheumatic heart disease. X-ray indicated posterior dilatation of auricles and a prominent pulmonary conus. Electrocardiogram showed an inverted T_4 consistent with myocardial damage.

As part of a general checkup 3 years later, intermenstrual bleeding was reported for 1 year, with spotting for 2 weeks. Pelvic examination was negative. A diagnostic dilatation and curettage were performed. A small amount of calcareous material was obtained.

After considerable technical difficulty a frozen section was made and diagnosed as calcified endometrium. The permanent sections microscopically showed plates of ossification of endometrial stroma similar to Case 1 (Fig. 3). Pathologic diagnosis was ossification of endometrium.

No information as to intake of vitamin D or calcium could be obtained.

Comment

Both of the cases reported showed generalized endometrial ossification as sequels of therapeutic abortions, performed because of recurrent hyperthyroidism and rheumatic heart disease, respectively. One patient had taken large amounts of vitamin D and calcium lactate for postoperative tetany after thyroidectomy. Since the parathyroid glands were not identified morphologically, they may have suffered postoperative vascular damage leading to hypoparathyroidism.

Endometrial ossification is not usually mentioned as a part of hypervitaminosis D. Sites of predilection for the metastatic calcification after excessive vitamin D intake are myocardium, arteries, lungs, gastric mucosa, kidney tubules, and connective tissues.[1, 2] In the two cases reported, reproductive physiologic changes in the uterus and local damage associated with induced abortions probably encouraged the calcific and osseous endometrial metaplasia observed.

In one instance there was a history of therapy with substantial doses of both calcium and vitamin D. The other patient had an incomplete history in this respect. It may be recalled that chemically the multiplication product of serum calcium and phosphorus must generally exceed 40, when both values are expressed in milligrams, before calcification will occur in osteoid. Vitamin D must also be present.[3] It is possible that sufficient excesses of any two of the three components, calcium, phosphate, and vitamin D, could lead to metastatic calcification. In other words, the second patient might have had excessive intake of calcium and phosphate, or metabolic abnormalities of kidney or parathyroid leading to the same increased internal concentrations predisposing to metastatic calcification.

Osseous metaplasia may represent a secondary reworking of calcified stroma, such as occurs in the calcified cartilage of bronchi in senility. In mixed mesodermal sarcomas (sarcoma botryoides), stroma ossification in the uterus is not uncommon. This is attributed to the multiple potentialities of malignant embryonic tissues. No embryonic or neoplastic processes were found in the cases reported.

Summary

Two cases of metaplastic endometrial ossification are reported. In one, the ossification was a manifestation of hypervitaminosis D. Both patients had previous therapeutic abortions. The basis of the endometrial bone formation is discussed.

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COLPOCERVICITIS EMPHYSEMATOSA

Report of a Case

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COLPOCERVICITIS emphysematosa is a very rare condition, usually associated with pregnancy and characterized by numerous gas-filled spaces beneath the mucous membrane of the ectocervix and vagina. The disease rarely gives rise to symptoms and is self-limiting.

Several reports of this condition occur in the European literature of the nineteenth century, the earliest being that of Hugier in 1847. In 1934, Ingraham and Hall[1] reviewed the literature and presented three cases of their own. After extensive investigation of these cases, two of which were in pregnancy, they were unable to establish a bacterial etiology. Attempts at identification of the gas contained within the cysts were unsatisfactory but they gained the impression that the gas was air.

Since their review several additional reports have appeared. Marshall and Bergstrom[2] described a case in 1935. Robberson and Owen,[3] in 1936, reported the disease occurring twice in the same patient. In 1948 Gardner[4] added another case and proposed a theory for the pathogenesis of the lesion. Bender and Jeffcoate[5] added two more cases in 1950 and postulated that the pathologic picture present resulted from epithelial downgrowths into the stroma; the epithelial cells became phagocytic and developed into giant cells which arranged themselves about a central gas-containing space. Neither Bender and Jeffcoate nor Gardner could offer a satisfactory explanation for the gas. As the cysts became distended with gas the giant cells and other leukocytes became compressed against the cyst wall and eventually disappeared. As the cyst enlarged it rose to the surface and ultimately burst spontaneously to disappear.

Since 1950 the only report that has appeared, to our knowledge, is that of Buchmann[6] who noted the similarity of the lesions in his case to those of a patient with "colpitis lipomatosa."

Most cases are reported under the heading of "vaginitis emphysematosa." In view of the fact that the ectocervix is usually involved as well as the vagina it is felt that "colpocervicitis emphysematosa" is the more appropriate term.

The etiology and pathogenesis of this condition remain a mystery largely because of its rarity, its evanescent nature, and the difficulties in analyzing the

Fig. 1. Fig. 2. Fig. 3.

Fig. 1.—Subepithelial inclusion of squamous cells with surrounding inflammatory cells. Several giant cells are also seen. (×300. Reduced one-third.)

Fig 2.—Numerous cysts are within the stroma, many in the deeper portion lacking cellular response. Other cysts contain giant cells and inflammatory cells. (×150. Reduced one-third.)

Fig. 3.—Periphery of a large intact cyst showing giant cells and inflammatory cells at border. (×300. Reduced one-third.)

contained gas. Many physicians, including gynecologists and obstetricians, remain unaware of its existence. For this reason and in accordance with the plea of Gardner the following case is felt worthy of report.

Case Report

G. F., a 26-year-old Negro woman, was admitted to the Medical Service of the Jewish Hospital of Brooklyn on Oct. 17, 1952, complaining of malaise, restlessness, chills, fever, and headache of several days' duration. Her last menstrual period occurred in September, 1952, and the flow was scanty. She could not remember the nature of her previous menses and denied the possibility of recent pregnancy.

Past history included four pregnancies, two resulting in spontaneous abortions and two in normal term deliveries. In 1949 she had been treated with penicillin at another hospital for secondary syphilis. At this time "multiple healing lesions of the cervix and vulva" were described. At previous and subsequent examinations in our outpatient clinic the cervix and vagina were found to be normal.

On admission her temperature was 103° F. She was alert and cooperative. Blood pressure was 106/52 and the pulse rate 120. Physical examination revealed only moderate diffuse lower abdominal tenderness.

The blood contained 10 Gm. of hemoglobin per 100 c.c. The red cell count was 3.89 million and the white cell count 7,350 per cubic millimeter. The differential white cell count was 84 per cent polymorphonuclear leukocytes, 14 per cent lymphocytes, and 2 per cent mononuclear cells. Urinalysis was negative. The Wassermann reaction was 4 plus. An Aschheim-Zondek test was positive.

Gynecologic consultation was obtained on the third hospital day. Pelvic examination revealed slight vaginal bleeding; the uterus was soft and enlarged to the size of eight weeks' gestation. No evidence of pelvic infection could be elicited. She continued to have a septic course and developed a pleural effusion. Treatment consisted of large doses of antibiotics and ACTH. On the sixteenth hospital day pelvic examination revealed the uterus to have decreased in size; bleeding was absent. The impression was that of a missed abortion. A repeat Aschheim-Zondek test was reported as negative. Her clinical condition gradually improved. Twelve days after the second pelvic examination, because of a recurrence of vaginal bleeding and the passage of dark blood clots from the vagina, she was taken to the operating room for curettage.

Just prior to the curettage, speculum examination revealed the cervix to be studded with innumerable blebs varying in size from 1 to 5 mm. in diameter. The blebs were noncrepitant but when one was pierced a "plop-like" sound was heard and no fluid exuded. Cervical biopsy was taken. The cervix was then dilated and curettage performed. The vagina was not inspected at this time.

One week later the cervical lesions showed signs of regression and upon inspection of the vagina the upper third was seen to contain gas-filled spaces similar to those seen in the portio vaginalis. The patient was then discharged from the hospital. She was next seen in the outpatient clinic one month later. She had no complaints. The cervix and vagina appeared normal on careful speculum examination.

Pathologic Report.—Cervical Biopsy: The ectocervical mucosa was considerably thickened and edematous so that intercellular bridges were prominent. Within the subepidermal stroma there were apparently detached groups of squamous epithelial cells. Several of these were bordered by an infiltrate composed of multinucleated giant cells, small and large round cells, occasional plasma cells, and polymorphonuclear leukocytes. Scattered throughout the stroma beneath the ectocervical mucosa there were cystic spaces varying markedly in size. In the larger spaces inflammatory cells and giant cells lay at the periphery while in the smaller cavities the cells lay in the center. Deep within the stroma empty spaces of small size were

closely packed and lacked any cellular infiltrate. The giant cells present in the more superficial spaces contained an eosinophilic cytoplasm and the nuclei were numerous and usually lay in the central portion of the cell. The endocervical glands did not appear unusual.

Curetted Material: This consisted of degenerated chorionic villi and clotted blood.

Diagnosis: Portion of cervix with cervicitis emphysematosa; degenerated placental tissue.

Summary

A case of colpocervicitis emphysematosa has been presented and the pathologic features illustrated.

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RECURRENT BLEEDING FROM THE VAGINAL VAULT FOLLOWING TOTAL ABDOMINAL HYSTERECTOMY

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VAGINAL bleeding is relatively rare as a complication of abdominal total hysterectomy. When it does occur, it can be most serious, requiring emergency treatment. This paper proposes, therefore, (1) to discuss a case of intractable vaginal bleeding following an abdominal total hysterectomy performed on the Gynecologic Service at the Hospital for Joint Diseases; and (2) to recommend, as an emergency lifesaving measure for such uncontrollable bleeding, the bilateral ligation of the internal iliac arteries.

The patient, G. J., a 42-year-old gravida i, para 0, Negro woman, was admitted to the hospital on Aug. 20, 1951, complaining of menorrhagia and intermittent backache of 4 months' duration, becoming progressively worse. Her last menstrual period had occurred 2 weeks prior to admission. Past history was notable only for the removal of a "pus tube" 20 years previously. Physical examination on admission revealed a midline abdominal scar. A tender mass was palpable in the lower abdomen rising 3 cm. above the symphysis. Pelvic examination revealed a 2 finger introitus, the cervix pointed posteriorly. The uterus was anterior, nodular, and irregular, enlarged to the size of a 10 weeks' gestation with a 6 by 8 cm. mass attached to the anterior wall. The admission diagnosis was myomas of the uterus.

On admission, the urine and serologic tests were negative, hemoglobin was 10.9 Gm., the red cell count 3.65 million, the white cell count 6,800, with normal differential. The sedimentation rate was 18 mm. in 45 minutes. Vaginal and cervical smears were negative for malignancy.

On August 23, a total abdominal hysterectomy and right salpingo-oophorectomy were performed under spinal anesthesia. A continuous lock stitch on the anterior and posterior vaginal cuffs was used for hemostasis and the vaginal vault was left open.*[1] The postoperative course was uneventful until the twelfth day, when the patient complained of pain in the right lower quadrant, weakness, and a foul purulent vaginal discharge. The blood count at this time revealed a hemoglobin of 7.7 Gm. with 2.1 million red blood cells. The coagulation time was 5 minutes, bleeding time 1 minute, platelet count 220,000. The prothrombin time was 20 seconds. The temperature was normal. The impression was a low-grade parametritis. The patient was transfused with 500 c.c. of blood, and antibiotic therapy was instituted.

On the fifteenth postoperative day, pelvic examination revealed an exquisitely tender mass in the posterior fornix. Three days later, on the eighteenth postoperative day, the patient began to bleed profusely from the vagina; on inspection the bleeding seemed to emanate from a necrotic vaginal vault. All clots were removed, and the vault and vagina packed tightly with Oxycel and plain gauze. Bleeding was controlled for 24 hours, following which the patient began to bleed through the packing. Her skin became cold and clammy, and blood pressure dropped to 80/60. She was treated for shock, and trans-

*Since Jan. 1, 1953, the operative technique employed on the Gynecological Service at the Hospital for Joint Diseases has been to close the vagina by approximating the anterior and posterior vaginal walls, leaving a small opening at the midline.

fused with 1,000 c.c. of blood. When the pressure rose to 120/80, she was taken to the operating room where, under general anesthesia, the packing was removed and the vaginal vault carefully inspected. The tissues about the vaginal vault were extremely friable, and the bleeding appeared to be a generalized ooze from the entire vaginal cuff. The cuff was resutured with interrupted figure-of-eight sutures and the bleeding controlled. The vagina was repacked and the patient transfused with 2,000 c.c. of blood. The packing remained dry, and was removed on the fourth day. Hemoglobin was 9.0 Gm. with a red blood count of 3 million.

Eight days later (the twenty-seventh postoperative day) sudden profuse vaginal bleeding recurred. The patient was immediately packed with Oxycel and plain gauze, and the bleeding was controlled.

The following day (9 days after the vaginal cuff was resutured) she again bled through the packing, and went into shock. The vagina was exposed and bleeding was visualized coming from high above the vaginal cuff on the left side. Since this point could not be reached, the vagina was packed very tightly and the abdomen was opened. At this stage, the patient's pulse and blood pressure were not obtainable, and active bleeding vessels could not be located. The pelvis was tightly packed, and the abdomen quickly closed. The patient was now receiving continuous transfusion.

Her blood pressure rose to 90/70, and she was returned to the ward. Thirty minutes later, as the pressure rose, she again began to bleed profusely through the vaginal packing, and again went into shock. She was given 2,500 c.c. of blood, and returned to the operating room, where the abdomen was reopened. Both internal iliac arteries were doubly ligated just distal to the bifurcation of the common iliac. The abdomen was quickly closed with through-and-through silk sutures. The vaginal packing was then removed, and no further bleeding noted.

The patient was discharged 1 month following the arterial ligation, after an uneventful postoperative course, in which there was no further vaginal bleeding, and during which she voided spontaneously. Bowel movements were also normal, without difficulty. At the time of discharge, the hemoglobin was 9.2 Gm. with a red cell count of 3 million.

She has been seen on several occasions in the follow-up clinic. She has gained weight; has no distress whatever in the gluteal regions after walking, and is asymptomatic. Six months postoperatively the hemoglobin measured 14 Gm. with a red cell count of 4.2 million.

Comment

Vaginal bleeding following total abdominal hysterectomy may be caused by one of several factors: (1) inadequate suturing, in which sutures have been allowed to loosen;[2] (2) inclusion of too much tissue in the suture, leading to necrosis and resultant slough 7 to 14 days later; (3) improper suturing of the lateral, or "bloody" angles of the vaginal cuff; (4) bleeding from the stump of the uterine artery, caused by slipping of a ligature or erosion into the uterine vessel by infection or carcinoma; (5) delayed or concealed bleeding following recovery from shock in prolonged procedures.[3]

To obviate these conditions, adequate hemostasis should be insured through tight ligatures, and double ligation of the large vessels. Before the patient leaves the operating room, the vagina should be inspected, and wiped out with sterile gauze so that any active bleeding may be detected and controlled while the patient is still under anesthesia. Recurrent bleeding after the patient has left the operating room requires packing of the vaginal vault with Oxycel and gauze under visualization, the packing to be left in place indefinitely.

If bleeding should recur after this, or if bleeding is massive at any time, it may originate from a large vessel or from many points. It then becomes imperative to open the abdomen and suture the bleeding points. If the tissues are friable, secondary to a low-grade infection such as parametritis, then bilateral ligation of the internal iliac arteries is recommended as a lifesaving measure.

Since this patient was treated, 6 more cases of similar ligation have been performed prophylactically following radical hysterectomy and bilateral lymphadenectomy for carcinoma of the cervix. The harmlessness of this procedure was borne out in each case; circulation of the rectum, anus, bladder, and perineum was not impaired.

Summary

1. A case of recurrent vaginal bleeding following total abdominal hysterectomy, treated by bilateral ligation of the internal iliac arteries, has been discussed.

2. The pathogenesis and treatment of vaginal bleeding following total abdominal hysterectomy have been summarized.

3. Ligation of the internal iliac arteries is recommended as a lifesaving measure for uncontrollable vaginal bleeding following total hysterectomy.

4. No impairment to the circulation of the rectum, anus, bladder, or perineum has been observed when this procedure is followed.

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ARTERIOVENOUS ANEURYSM OF THE UTERUS

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ARTERIOVENOUS aneurysm of the uterus is so rare that it would deserve only casual consideration as a gynecologic curiosity if the lesions were not so extremely serious to the patient. In none of the three cases previously reported was the diagnosis established before operation: one[1] of these patients died, another[2] recovered with residuals of hemiplegia, and the third[3] was near death from massive uterine hemorrhage as a result of instrumentation before operation and again from massive intraperitoneal hemorrhage postoperatively. Elkin and Bonner[4] reported a case involving the right uterine vessels five months after hysterectomy which was diagnosed preoperatively.

Arteriovenous fistulas in general almost always follow trauma, usually of the penetrating type. These phenonema usually occur in sequence: (1) dilatation of the vein and its tributaries; (2) hypertrophy of these veins; (3) damage to the adjacent valves; (4) dilatation of the artery proximal to the fistula; and (5) cardiac manifestations. Symptoms are: (1) a murmur, continous in type, increased with systole, transmitted centrally along the vein and of maximum intensity over the site of the lesion; (2) a thrill, which is merely the tactile manifestation of the processes involved in the murmur, the timing and location being similar; (3) venous pulsation, most marked at the site; (4) hemorrhages about the site; and (5) edema and trophic disturbances if peripheral vessels of an extremity are involved. Branham's sign, marked slowing of the pulse, occurs when the abnormal communication between the artery and vein is occluded.

Case Report

An unmarried white gravida 0, aged 34 years, was seen Oct. 1, 1939. She was underweight and quite pale. Her past history was irrelevant except for an operation for ruptured cyst of the ovary in 1929 at which time the appendix was removed. She had had severe menorrhagia for 2 years. Three episodes of bleeding had been serious enough to require curettage, packing of the uterus, and blood transfusions. On one occasion spontaneous bleeding was so alarming that I hastily packed the uterus in my office with gauze bandage, the only material available. Treatment with thyroid, estrogens, and testosterone plus supportive measures was without benefit.

Blood pressure was 115/50 and pulse 90. Skin and mucosa were pale but there was a slight malar flush. A systolic murmur, well transmitted to the right side of the neck and to the apex of the heart, was present. A harsh thrill was felt over the precordium, the base of the neck and both femoral arteries. It could be diminished by pressure over the right subclavian vessels but the pulse was not slowed thereby. The abdomen was essentially normal except for the thrill and bruit over both inguinal regions. Pelvic examination showed normal external genitals with marital outlet. The cervix pointed to the

introitus and was fixed to thickened nodular uterosacral ligaments. Tender nodules typical of endometriosis were present in the cul-de-sac. The uterus was fixed in retroversion and appeared to be normal in size. Both adnexa were nodular and fixed. A pulsating thrill could be felt over both uterine arteries which was unaffected by pressure on the great vessels of the neck. On inspection both fornices of the vagina were seen to pulsate. Simultaneous pressure on both fornices failed to slow the pulse.

Fluoroscopic examination of the heart and electrocardiograms were reported normal by Dr. T. Sterling Claiborne, who thought the cardiovascular findings to be organic in nature and probably due to congenital defect in the mediastinum, although he conceded the possibility of arteriovenous fistula in the pelvis.

Laboratory data: Analysis of the catheterized urine specimen was normal; the red blood count was 2.8 million, hemoglobin 7.3 Gm., white cell count 8,600; the sedimentation rate was normal. Preoperative diagnosis: endometrial hyperplasia (previous curettings), pelvic endometriosis, and arteriovenous fistula, either pelvic or mediastinal.

Operation: After transfusions the cervix was deeply cauterized preliminary to the opening of the abdomen through a Pfannenstiel incision. The uterus was normal in size, fixed in second-degree retroversion. Its color was dusky, resembling pregnancy, and the consistency was soft. The entire organ and the adjacent uterine and ovarian vessels pulsated with a strong thrill. The vessels were dilated and tortuous. The uterus was densely adherent to the sigmoid and parietal peritoneum through nodules of endometriosis, most of which spurted profusely on being separated. The left ovary was enlarged to 4 by 6 cm. with blood-filled cysts. The right ovary was only slightly enlarged but its surface was puckered with occasional small, black, stellate lesions. Both broad ligaments were peculiar in that the so-called avascular area in each presented a triangular fenestra bounded laterally by the pelvic wall, superiorly by the tubes and round ligaments, and inferiorly by the cardinal ligaments and uterine vessels.

Supravaginal hysterectomy, bilateral salpingectomy, and right oophorectomy were carried out with great difficulty in hemostasis. Transfusion of 600 c.c. of whole blood was given postoperatively. Convalescence was rapid and the patient left the hospital on the seventh day. A mild parametritis developed on the tenth day which responded to conservative therapy.

Pathologic report (Dr. W. B. Matthews): The uterus, amputated above the cervix, measured 5.7 by 5.2 by 5.2 cm. It was symmetrical and covered by rough adhesions. The wall was soft and contained many dilated blood sinuses and numerous bluish cystic spaces. These were probably small endometrial implants. The mucosa was very thin and looked as if it had been recently packed with gauze. At one point it seemed as if the endometrium was invading the uterine wall. Two small fibroids were present. The ovary measured 4 by 6 cm. and was partly calcified. *Microscopic:* Sections of the endometrium showed this layer to be almost absent, having been recently exfoliated. The few glands remaining were in the early proliferative phase. In several sections of the myometrium there were islands of endometrial mucosa. Some of the glands were dilated and cystic and they were surrounded by typical endometrial stroma. A peculiarity of the myometrium was the large number of extremely dilated blood spaces. This was no doubt due to a circulatory disorder. Sections of the blood-filled cyst of the ovary failed to show any endometrium. It was probably an old luteal cyst rather than endometriosis.

Final diagnosis: Small fibromyomas of the uterus; adenomyosis; endometriosis of the pelvic peritoneum; congenital fenestration of the broad ligaments; arteriovenous fistula in the uterus and old hemorrhagic corpus luteum cyst of the right ovary.

The patient has remained comfortable, has married, and states that sex relations are normal and painless. The left ovary is definitely nodular and slightly increased in size. The blood count returned to within normal limits. The heart murmur improved very rapidly after operation and has now disappeared completely. The femoral thrill ceased immediately and the precordial thrill is no longer present. Dr. Claiborne reports the vascular system to be entirely normal.

Comment

Dilatation and curettage or other instrumentation of the uterus in the presence of signs or symptoms of arteriovenous fistula is extremely hazardous and probably should never be performed. If such procedures are considered mandatory, the operating room should be prepared for immediate hysterectomy with a generous supply of blood available should this become necessary. Operation is a matter of considerable hazard and in all cases has been characterized by difficulty in controlling bleeding. The postoperative course has been complicated in every case. The rapid recovery of this patient despite obviously inadequate replacement of blood was possibly due to stabilization of the blood volume which has been found significantly increased in patients with arteriovenous fistula of long duration.[5] The reduction in blood volume following operation is accomplished by decrease in the fluid component wth corresponding concentration of the cellular elements.

Addendum.—Since this paper was submitted for publication, another case of arteriovenous aneurysm of the uterus has been reported: Gaines, J. A., and Greenwald, J. C.: Am. J. Obst. & Gynec. 65: 997, 1953.

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HIRSUTISM AS THE ONLY CLINICAL MANIFESTATION OF AN ADRENAL ADENOMA*

A Case Report

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HIRSUTISM unaccompanied by other signs of virilization in women in most instances in the past has been attributed to idiopathic causes without thought of possible adrenocortical pathology as the underlying etiology. Kinsell and Lisser,[1] however, recently reported upon a patient with hirsutism unaccompanied by other signs of virilism, such as enlargement of the clitoris, deepening of the voice, amenorrhea, etc., but who had fairly marked elevation of the total 24 hour 17-ketosteroid excretion. Further study revealed the presence of a unilateral adrenal tumor. Postoperatively, there was a return of the 17-ketosteroid excretion to normal levels, with some regression in the hirsutism three years later.

We have had the opportunity to study a similar case and are presenting it for the purpose of emphasizing how an adrenocortical adenoma may be present without producing the full clinical picture of virilism.

P. B., No. 112472, a 23-year-old unmarried white woman, a physiotherapist, was first seen in the Presbyterian Hospital in October, 1952, complaining of excessive hirsutism.

At the age of 15 years the patient first noted excessive growth of hair on the face, arms, legs, and pubic region which persisted and finally became worse just prior to admission. She had her menarche at 14½ years of age, and since that time up to the present, had had perfectly normal menses every 22 to 28 days, lasting three to four days. During this period there was no evidence of acne, deepening of the voice, flattening of the breasts, change in libido, etc. Her weight persisted at 160 pounds. There had been no change in appetite and no increased muscular development. There was no familial history of hirsutism. The remainder of the history was essentially noncontributory.

Physical examination revealed a moderately obese, large-structured, hirsute, white, olive-skinned woman who appeared neither acutely nor chronically ill. She had a normal pulse and temperature and her blood pressure was 128/80. The pertinent physical findings were limited to the hirsutism. She had long, dark hairs over her face (Fig. 1), as well as on the arms and legs, and there was a male pubic escutcheon. There was no enlargement of the clitoris, and the breasts were within normal limits. Pelvic examination revealed a normal uterus, ovaries, and tubes.

*Supported in part by grants from the American Cancer Society, as recommended by the Committee on Growth, and the United States Public Health Service.

**Fellow of the American Cancer Society.

The laboratory findings, which included a hemogram, urinalysis, serum sodium, potassium, chloride, carbon dioxide and uric acid determinations, and a glucose tolerance test, were all normal. Prior to admission a 24 hour urine specimen contained 50 mg. of 17-ketosteroids.

A presacral aerogram revealed the presence of a large mass in the left adrenal area depressing the upper pole of the left kidney (Fig. 2). Intravenous pyelogram confirmed this. X-rays of the skull and chest were completely negative.

Fig. 1.—Patient P. B. Demonstrates facial hair.

After a suitable control period 200 mg. per day of cortisone was administered intramuscularly for four days to note its effect on the total daily 17-ketosteroid excretion in the manner reported by Wilkins,[2] Bartter,[3] and Jailer.[4] As expected, there was no fall in the 17-ketosteroid excretion (Table I). In addition, the urinary neutral extract was tested for dehydroisoandrosterone in the manner described by Allen.[5] A value of 24.6 mg. of dehydroisoandrosterone was obtained which denotes a very significant elevation. For confirmation another 24 hour urine specimen was chromatographed according to the method of Devis[6] and the various fractions identified by infrared spectrophotometry through the courtesy of Dr. Seymour Lieberman. This revealed significantly elevated amounts of dehydroisoandrosterone and androsterone (Fig. 3). The estrogen excretion[7] preoperatively was noted to be markedly elevated with a value of 350 gamma per 24 hours. Pregnanediol excretion[8] (about two weeks prior to menstruation) was 5.3 mg. per 24 hours which was within normal limits.

On Oct. 24, 1952, an excision of the left adrenal tumor was performed. Within three days of the operation her total daily 17-ketosteroid excretion fell to normal values and has since remained at these levels. Pregnanediol excretion was 1.3 mg. per 24 hours which again was normal. Estrogen excretion fell to 68.8 gamma per 24 hours which is essentially at the upper limit of normal. Repeat column chromatographic analysis revealed an absence of dehydroisoandrosterone, a decrease in the amount of androsterone, and a decrease in the amount of etiocholanolone and 11-keto-etiocholanolone (Fig. 3). Pathologic examination of the adrenal tumor showed it to be a benign adrenal adenoma of the adrenogenital syndrome type.

Her postoperative course was quite uneventful, and though there was no marked regression in the hirsutism, it was possible to pull several hairs from her face quite easily several days after surgery. On subsequent visits, eight months postoperatively, the patient was noted to have plucked hair from her face which never again returned and clinically she looked much improved.

Fig. 2.—Presacral aerogram demonstrates large left adrenal mass which is depressing the upper pole of the kidney.

TABLE I. RESPONSE OF 17-KETOSTEROIDS TO CORTISONE ADMINISTRATION

DATE	MEDICATION	17-KS., MG./24 HR.
8/28-8/29/52	Control	50.0
10/13-10/14	Control	68.0
10/17-10/18	Control	50.0
10/18-10/19	Cortisone, 200 mg./day	81.4
10/19-10/20	Cortisone, 200 mg./day	95.0
10/20-10/21	Cortisone, 200 mg./day	52.1
10/21-10/22	Cortisone, 200 mg./day	67.5
10/24	Removal of adrenal tumor	
10/27-10/28	Postoperative	8.46
10/28-10/29	Postoperative	10.1
10/31	Postoperative	4.7
11/3	Postoperative	4.6
6/9/53	Postoperative	8.4

Comment

Hirsutism as the only manifestation of virilism due to underlying adrenal cortical tumor is a rarity. To our knowledge the only other reported case is that of Kinsell.[1] Unquestionably, most cases of hirsutism are simply constitutional or familial in character. Slightly elevated 17-ketosteroid values may be encountered in such cases. However, further investigation of these patients usually reveals no discernible pathology, but, in the rare case, as in the present instance, an adrenal tumor may be discovered. This in itself justifies the use of 17-ketosteroid studies as a routine screening procedure in hirsute patients.

In those instances where the evidence for an adrenal tumor is substantial but not complete, the "cortisone test," namely, the response of the urinary

17-ketosteroids to cortisone administration is a useful adjuvant in the differential diagnosis between adrenal hyperplasia and tumor (Jailer and associates[4]; Gardner and Migeon[9]). An adrenal tumor, probably because of its independence from pituitary control, does not reflect depression of ACTH production by cortisone, and thus there is no fall in the total daily 17-ketosteroid excretion. This patient showed the characteristic lack of response of an adrenal tumor.

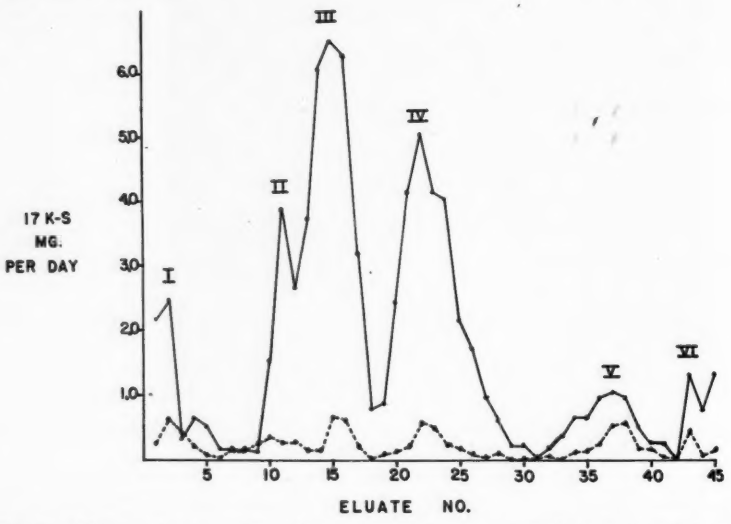

Fig. 3.—Chromatogram of urinary neutral extract before and after operation. Preoperative values are shown with solid line; postoperative findings with broken line. *I*, Artifact. *II*, Dehydroisoandrosterone. *III*, Androsterone. *IV*, Etiocholanolone. *V*, 11-keto-etiocholanolone. *VI*, Artifact.

Allen[5] and others have stated that, normally, dehydroisoandrosterone, a beta-ketosteroid, makes up about 10 per cent of the total 17-ketosteroid excretion. However, in the presence of adrenal tumor this fraction comprises upward of 50 per cent of the total. On this basis the Allen test was devised as an easy method of detecting this increase although it is not specific. In this case dehydroisoandrosterone made up 49 per cent of the total, and a positive Allen test was obtained. As confirmatory evidence a significant increase in the dehydroisoandrosterone fraction as well as the androsterone fraction was demonstrated spectrophotometrically. Postoperatively, chromatographic analysis of the urine showed a disappearance of dehydroisoandrosterone, and a decrease in androsterone and etiocholanolone, showing the tumor to be the source of the increased excretion of these 17-ketosteroid fractions. Estrogen excretion also showed a marked decrease after the successful removal of the adrenal adenoma. This has been reported previously (Jailer[7]; Dohan and co-workers[10]). Pregnanediol excretion showed no statistically significant change other than what might occur with variations in the menstrual cycle.

It is interesting to note at this point that a patient whose adrenal glands were producing such large amounts of androgen had neither interference with her normal menses nor other signs of virilism such as enlargement of the clitoris, increased muscular development, change in voice, etc.

Summary

A case exhibiting hirsutism as the only clinical manifestation of adrenal adenoma, associated with elevated total daily 24-hour urinary 17-ketosteroid excretion, is presented. A marked elevation in the beta fraction of the total 17-ketosteroids, dehydroisoandrosterone, was noted.

The importance of the routine determination of 17-ketosteroids to exclude adrenal virilism in patients with apparently "idiopathic" hirsutism is stressed.

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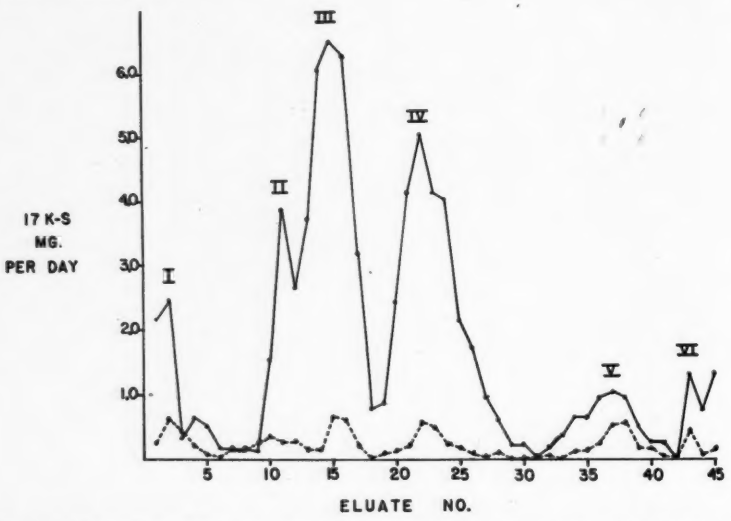

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A DUAL-PURPOSE CANNULA FOR THE CYTOLOGIC METHOD*

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THIS article proposes to introduce an improved glass cannula designed for taking both vaginal and endocervical smears for cytologic study. As a practical improvement this cannula (1) simplifies the technique of obtaining exfoliated cells from the female genital tract, and (2) obviates the problems involved in taking the cervical smear, particularly in regard to the cervical scraping.

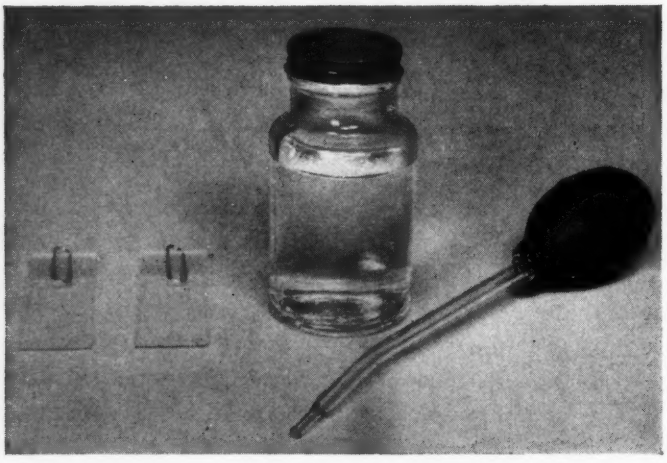

Fig. 1.—Dual-purpose cannula showing the tapered end which can be used for both vaginal and endocervical aspiration.

The initial use of the cervical scraping was based on the premise that cancer of the cervix originated at the junction of the ectocervix and endocervix. Adenocarcinoma of the cervix, however, arises in the columnar cells within the cervical canal. Even more commonly, epitheliomas arise in the canal, possibly from isolated islands of squamous epithelium or from metaplastic areas. If the lesion originates within the canal, it will be missed by a cervical scraping, which removes only the superficial cells from the junction of the endocervix and ectocervix. A cervical scraping, furthermore, may fail to show cells derived from endometrial lesions. Regardless of the type of instrument em-

*Designed by George O. Richardson for the Ortho Research Foundation, Raritan, N. J.

ployed, the cervical scraping removes a rather thick layer of tissue which dries rapidly when placed on a glass slide. Drying of material results in distortion of the nuclei and cytoplasm, and, not infrequently, after standard staining, is reflected in large blown-up nuclei as well as other variations in size and shape. Thus false cytologic interpretations, even false positives, are the possible end products of the cervical scraping, a method of obtaining material which violates some of the concepts of exfoliation in cytologic studies.

In order to resolve these difficulties, an improved reinforced glass cannula has been developed (Fig. 1). Its double thickness renders it virtually unbreakable in the vagina. Because of its tapered end, it lends itself not only to vaginal-smear taking, but to the taking of endocervical aspiration smears. The convenience of using a single instrument is obvious, but the chief value of this cannula is that it makes it possible to discard the cervical scraping for the more reliable endocervical aspiration smear, which not only obtains material from endocervical and ectocervical areas, but also yields exfoliated cells coming from the endometrial cavity.

The improved dual-use cannula, now in use at Bellevue and University Hospitals of New York University-Bellevue Medical Center, has been found superior to the original vaginal pipette, and an advance in the practical application of the cytologic method.

A NEW VAGINAL AND CUL-DE-SAC RETRACTOR*

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IN THE course of performing a vaginal hysterectomy one frequently uses a retractor placed through the posterior fornix and into the cul-de-sac, in order to get better exposure for the clamping, cutting, and suturing necessary in the operation.

The customary retractor now employed has the following features as shown in Fig. 1, *A*:

1. The weight of the retractor is rather uniformly distributed or in some is heavier in the handle than in the blade.

2. The angle between the blade and handle is 90 degrees.

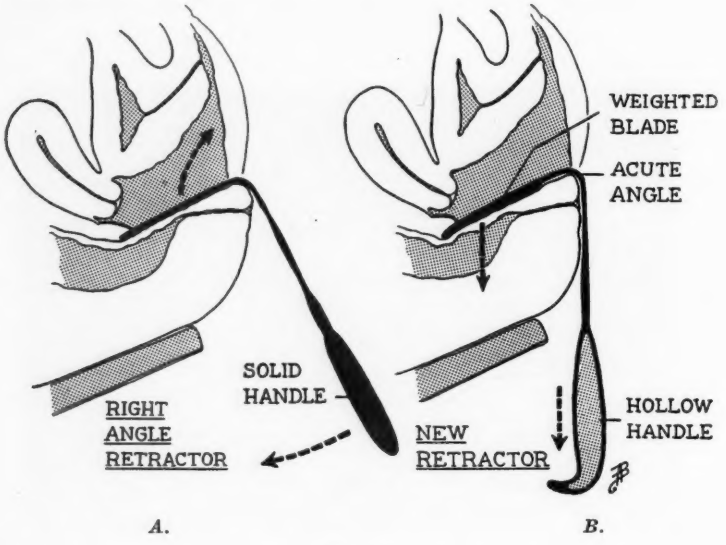

Fig. 1.

As a result of these features, when the retractor is inserted and especially when the patient is put into the Trendelenburg position to keep the intestines out of the operative field, there is a great tendency for the retractor to fall out as the handle swings by gravity toward the vertical, as shown in the diagram.

In the new instrument (Fig. 2), by (1) placing the weight almost fully in the blade, (2) lengthening the blade, and (3) hollowing the handle and grinding it down further to remove as much weight therefrom as possible, along with (4) changing the angle from a right angle to an acute angle, the following is accomplished (Fig. 1, *B*):

Here, by comparison, are the weighted, lengthened blade, the acute angle, and the hollow light handle in position. It can readily be seen that the pull now is directly downward mainly in the weighted blade and also in the handle, the latter especially hanging directly

*Presented at a meeting of the Chicago Gynecological Society, May 15, 1953.

vertically when the patient is placed in the Trendelenburg position. There is no possibility of the instrument's falling out or dropping out when touched as frequently happens with the customary retractor.

Incidentally, it has also been found that, in using this new retractor, the slight additional pressure has a tendency to diminish the amount of posterior cuff vascular oozing.

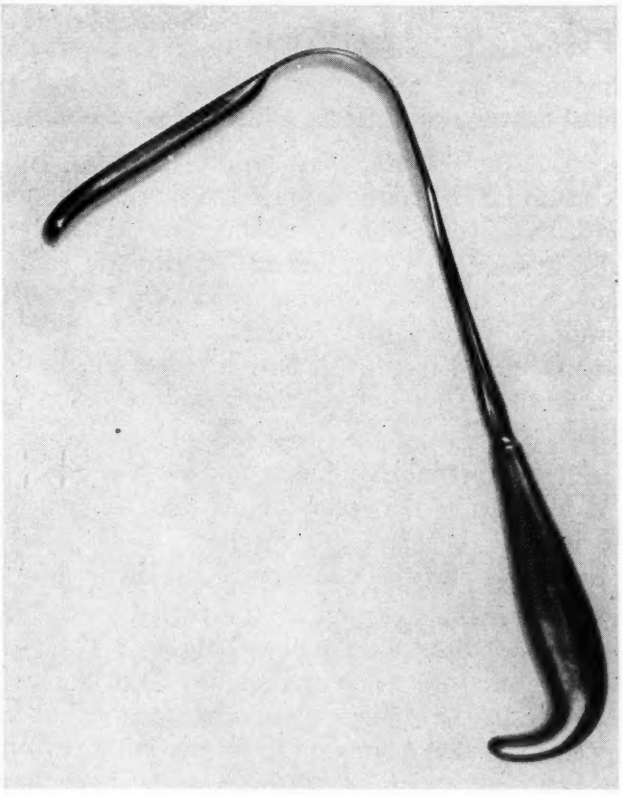

Fig. 2.

In conclusion, here is a real self-retaining vaginal and cul-de-sac retractor which appears to be an improvement over the instrument now used.

30 N. Michigan Avenue

Editorial

Fetal Salvage in Patients With Diabetes Mellitus

THE correspondence in this issue concerning the fetal salvage in patients with diabetes mellitus is of considerable importance. The number of women with diabetes mellitus is constantly increasing and naturally the number of pregnancies is also increasing. This increased birth rate has also affected the number of patients with diabetes, because the disease frequently first becomes manifest in pregnancy. Obviously, internists who have specialized in the treatment of patients with diabetes will have a larger number of patients with severe diabetes than will be encountered in an average obstetrical service.

Much has been written about the occurrence of pre-eclampsia or toxemia in the diabetic patient. Unfortunately, edema is a very common finding in pregnant patients. It is probable that some of the diabetic patients did not have pre-eclampsia or toxemia but had intercapillary glomerulosclerosis, with its accompanying proteinuria and the associated ophthalmoscopic findings.

At the Chicago Lying-in Hospital in the period from 1931 to 1952, 119 patients with diabetes mellitus were followed through 170 pregnancies. Two patients died, one from diabetic coma and another from puerperal sepsis. The uncorrected pregnancy loss, including abortions, amounted to 21 per cent, but for babies that weighed 1,000 grams or more the stillbirth and the neonatal mortality was 16 per cent, which is still over seven times that for the whole hospital. The edema, proteinuria, or hypertension of varying degrees resulted in a diagnosis of toxemia of some sort in 24 per cent of the cases. Hormone therapy was used on only six patients.

The cases of diabetes in pregnancy seen at the Sloane Hospital for Women were reviewed in this JOURNAL in 1951. During the 27 years studied, 112 patients were followed through 147 pregnancies. Excluding 12 early spontaneous and 28 therapeutic abortions, there were 107 pregnancies, with a gross fetal mortality of 20.7 per cent. Further elimination of 3 late abortions resulted in a mortality of 18.3 per cent among 104 viable infants. Finally, excluding the 12 patients with viable infants, who received inadequate antepartum care, a highly corrected fetal mortality of 7.6 per cent would result.

Hypothetical as this sort of reasoning is, it does: (1) emphasize the importance of meticulous antenatal supervision of the pregnant diabetic patient, and (2) offer an alternative explanation to the results achieved by endocrine therapy. None of the patients were treated with hormones. Poor control of the diabetes was thought to account for most of the fetal loss, though a toxemia rate of 32 per cent was contributory. The cesarean section rate at the Sloane

Hospital in this group was 16 per cent. If 75 per cent of the patients who reached the thirty-seventh week had been sectioned, about 50 additional sections would have been done, with a maximum theoretical salvage of 5 more babies. With 16 per cent sections, however, only 10 per cent of the fetal deaths were in the neonatal period, as opposed to more than 50 per cent neonatal deaths among those with a 75 per cent section rate.

We are, as yet, unconvinced that endocrine therapy or elective cesarean section can improve the fetal prognosis of a pregnant diabetic patient or in any way improve the results obtained with good antenatal care.

The reports of Ferguson and of Dieckmann and associates, on the routine use of graduated doses of stilbestrol to pregnant patients beginning before the twentieth week, according to the Smiths' technique, demonstrated that this hormone had no effect on decreasing the incidence of pre-eclampsia, of hypertensive disease, or of the unseparated group of so-called toxemias. The experience at the Chicago Lying-in Hospital has been that whenever patients are cooperative the results for mother and baby are better. Frequently the figure is significant when compared with that for the hospital as a whole, as well as for the group of uncooperative patients.

The results without hormone therapy from the maternity services with which the editors are associated are similar to some reported statistics. However, other investigators report better results with the use of hormones. Some method of separating the pregnant diabetic patients according to the duration and severity of the disease is necessary. The White classification should be used until more data are available. The results from several services could be pooled, or each case of diabetes in pregnancy could be registered with a central agency, such as our Academy.

The Editors.

Department of Reviews and Abstracts

CONDUCTED BY GEORGE W. KOSMAK, M.D., NEW YORK

Selected Abstracts

Cancer, Malignancies

Krug, A. P.: Cervical Cancer and Pregnancy, Bol. Soc. chilena de obst. y ginec. 13: 77, 1952.

A critical study of 9 cases of carcinoma of the cervix complicating pregnancy is reported by the author. There was a variety of therapeutic approach, only 2 cases having been treated the same way. Unfortunately 8 of the 9 patients were dead when this paper was written. There was a 44 per cent incidence of cases classified as Stage III. The author, therefore, cannot help but believe that pregnancy stimulates cancer malignancy, this in spite of different opinions from other clinics. Viability of the child was the most important factor in determining the therapeutic approach. Next in importance was the extension of the growth. The author believes that the diagnosis of cervical carcinoma is made too late when pregnancy is present, this being the most important reason for the high incidence of Stage III in his series.

RICARDO L. GORBEA

Ruiz, Rivas M.: Actual Problems Encountered During Roentgen Treatment of Uterine Cancer, Acta ginec. Madrid 4: 47, 1953.

The author in this paper reviews the techniques used by European and American clinics, inserting his own personal views and procedures. As chief of the Provincial Hospital of Madrid, Department of Radiology, the author controls the techniques used at this hospital and has arrived at some definite ideas as to the value of preradiation preceding radium therapy. He also suggests the use of deep therapy preceding any major dramatic procedure in the surgical field. After analyzing Kaplan's and Corscaden's method of treatment he concludes his paper by stating that in spite of all the progress made in this line, the solution of the cancer problem will not be found in the fields of surgery or roentgenotherapy, but through the study of microbiology, medical pathology, and the further knowledge of the ultravirus, together with an understanding of the importance of the mesenchymal tissue, particularly the reticuloendothelial system.

RICARDO L. GORBEA

Zuckermann, Conrado: Hydatidiform Mole and Choriocarcinoma With Peculiar Characteristics, Rev. mex. de cir., ginec. y cáncer 20: 295, 1952.

The author reports on two interesting cases, one a hydatidiform mole in a 54-year-old patient, and the other a markedly neoplastic and rapidly growing choriocarcinoma in a patient 22 years old. The mole presented many diagnostic possibilities, due to the age of the patient. However, the eventual treatment of the condition with total hysterectomy brought about a complete cure. The patient is alive and doing well three years following surgery.

The case of choriocarcinoma was reported because of its rapid course, the patient dying two months after radical hysterectomy and nine and one-half months following her pregnancy. Before laparotomy, this patient was repeatedly curetted but no pathological examination of the curettings was done, because it was thought the bleeding was caused by retained secundines. The author feels that the patient might have been saved if an earlier diagnosis had been obtained.

RICARDO L. GORBEA

Arenas, N., Guiroy, A. J., Costa, N. P., Ahumada, J. C., Sammartino, R., Dionisi, H., Pecorone, R., Chevalier, R., and Wood, J.: Symposium on Hydatidiform Mole and Choriocarcinoma, Bol. Soc. de obst. y ginec. de Buenos Aires 31: 426 and 451, 1952.

This symposium was carried out as an extraordinary session of the Buenos Aires Obstetrical and Gynecological Society, the first two papers dealing with the etiopathogenesis, clinical symptoms, diagnosis, and treatment of hydatidiform mole. These two papers are well illustrated with charts and tables and a bibliography covering most of the world literature. A review of 67 cases is presented, showing that only 4 patients (6.95 per cent) died. These statistics cover a period ranging from 1928 to 1951, with deliveries numbering 140,434. The treatment of the mole is dependent upon the concentration of gonadotropins in the blood serum following emptying of the uterus. If the gonadotropins do not disappear but instead are markedly increased, the authors believe this to be a sure sign of reversal to choriocarcinoma and the treatment then should be radical extirpation.

The rest of the papers, six in number, touch on the pathogenesis of choriocarcinoma, its symptomatology, anatomical pathology, hormonal diagnosis, clinical syndrome, and its treatment, the treatment being the surgical approach with radical definitive procedures followed by radiation therapy. Radiotherapy is used for palliative purposes when diagnosis is made too late. Choriocarcinoma is not sensitive to curietherapy. The papers on choriocarcinoma are well illustrated with charts and tables and the bibliographical references are multiple.

RICARDO L. GORBEA

Barnes, Allan C., and Rothchild, Irving: Experimental Use of Intravenously Administered Progesterone in Advanced Cases of Cervical Carcinoma, Obst. & Gynec. 1: 147, 1953.

This is the first report of long-continued progesterone administration by the intravenous route. Progesterone in doses ranging from 100 to 500 mg. was given daily for 10 to 20 days to 12 patients with recurrent Stage II squamous cancer of the cervix. X-ray irradiation was given concurrently. Some received penicillin and heparin as well. There was no significant retardation in the progression of the cancer. The commonest complication was thromophlebitis.

WILLIAM F. FINN

Blaikley, J., Lederman, M., and Lewis, T.: Results of Treatment of Cancer of the Cervix, Lancet 2: 950, 1952.

A joint clinic was set up between the Chelsea Hospital for Women and the Royal Cancer Hospital to manage carcinoma of the cervix. Between 1944 and 1946, inclusive, 102 patients were treated by radiotherapy, 16 by Wertheim hysterectomy, and 7 by other methods. The Stage I and II patients received radium by a modified Stockholm technique with 50 to 60 mg. in the uterus and 30 to 75 mg. in the vaginal vault for 22 hours. Three insertions were made with a week between the first and second and two weeks between the second and third. This was followed by external radiation with a 400 kv. machine. The tumor doses were not expressed. Stages III and IV patients received external radiation first and a modified application of radium later.

The results of radiotherapy with patients excluded who died of intercurrent disease are as follows: Stage I, alive and well after 5 years, 56 per cent, Stage II, 53 per cent, Stage III, 14 per cent; no survivals of Stage IV; over-all survival rate 40 per cent. Eleven Stage I, 4 Stage II, and 1 Stage III were managed surgically. Sixty-four of the Stage I, 25 per cent of the Stage II, and the only Stage III survived five years. The over-all survival was 56 per cent.

These results were compared with the years 1936 to 1943. During this time, the combined clinic was not functioning. Thirty-nine of Stage I, 28 per cent of Stage II, 15 per cent of Stage III, and 3 per cent of Stage IV with an over-all of 22 per cent were alive and well after five years.

The gratifying improvement in the latest series was attributed to more meticulous care, the joint clinic, and wider experience of the team of gynecologist and radiotherapist.

THOMAS L. BALL

Graham, John Barkley: Histologic Grading of Cancer of the Uterine Cervix, Surg., Gynec. & Obst. 96: 331, 1953.

All of the methods used for grading are ways of estimating and expressing the degree of anaplasia. The practical object of histologic grading is to predict the outcome of a particular form of treatment. The technique is partially subjective and limited to the biopsy which may or may not be a good sample of the tumor. The same observer may change the grade from time to time, especially in borderline cases. Of greater importance is the difference in interpretation of different observers. The degree of anaplasia correlates poorly with the clinical extent of the disease when the patient is first seen but somewhat better with the incidence of metastases in postmortem material. Radiotherapy results in a moderately higher cure rate in differentiated tumors than in anaplastic ones. It is concluded that histologic grading is of limited prognostic value in cancer of the cervix.

WILLIAM BERMAN

Endocrinology

Foss, G. L.: The Influence of Androgens on Sexuality in Women, Lancet 1: 667, 1951.

A study of the sexual behavior of women who were being treated for advanced breast cancer with massive doses of testosterone was made. Ten patients with advanced mammary carcinomatosis were treated with doses of testosterone propionate which varied between 200 and 300 mg. daily. During this treatment a considerable and abnormal increase in sexual desire was noted in those patients who had shown general clinical improvement. The observations in this series confirm the earlier findings of numerous other workers on the effect of androgens on sexual behavior in females and are in accord with the experiments of Klein on animals.

It is suggested that androgens may possibly be the normal factor influencing sexual behavior in both male and female, the added gonadal androgen being responsible for the aggressive male sexual behavior. In the female, the state of receptivity to the male may normally be controlled by adrenal cortical androgens and considerably augmented by exogenous androgens. The author, therefore, feels that sexual behavior in the female may normally depend more on suprarenal androgens than on estrogens.

IRVING L. FRANK

de Guerrero, Carlos: The Estrogens in the Treatment of Repeated Abortions, Ginec. y obst. de México 7: 493, 1952.

The author in this paper reviews all possible causes that might bring about the clinical picture of repeated abortion. He enumerates also all the material that is at the disposal of the clinician to make an etiological diagnosis of repeated abortion. A review of

the principal factors on which the treatment of repeated abortion by estrogens has been justified is further made and evaluated. The author touches on the theories and facts that explain the modus operandi of the estrogens in the prevention of abortions.

In presenting his statistical data on cases personally treated he has selected those cases which were actually cases of hormonal imbalance which were clinically proved. The technique followed was that used by the Smiths, with an occasional variation in cases of threatened abortions.

Finally, of 116 cases that were studied, there were 65 cases, 56 per cent, classed as caused by hormonal deficiencies. In this group there were obtained 48 pregnancies of over 7 months' gestation, equivalent to 70.38 per cent of success, with 7 failures in which treatment was instituted too late and 10 cases wherein treatment met complete failure. The estrogen treatment was also instituted prophylactically in 43 cases as a preventive measure, with a total salvage of 35 cases, 81.4 per cent.

The author closes his paper with the following conclusions: (1) The use of estrogens (diethylstilbestrol) does not produce abortions. (2) On the contrary it promotes the action of the corpus luteum and the placenta, contributing in this way to prevent abortions. (3) Estrogens are of definite value in treating cases of threatened abortions. (4) Estrogens should be used in cases of pregnancies in women with known hormonal deficiencies.

RICARDO L. GORBEA

Gomez Maestro, D. V., and Botella Llusia, J.: Intermediary Metabolism of the Androgens in Normal Females: A Hypothesis on Its Physiologic Significance and Its Mode of Action, Acta ginec. Madrid 4: 9, 1953.

Testosterone injected into females is recovered in smaller quantities than when it is injected into males. The author believes there is an endogenous disappearance of the testosterone and its maximum is reached during the luteal phase of the menstrual cycle in adult females. Because of the fact that equivalent quantities of pregnandiol appear in the urine during this phase, it is believed that the corpus luteum is capable of metabolizing the testosterone or any of its intermediary products into progesterone. A hypothesis is therefore created in which the author believes that the work of the androgens in mature adult women can be explained by the formation of by-products of the androgens during the luteal phase of the menstrual cycle.

The fact that androgens are normally found in the urine and blood of adult women makes the author believe that their function is to balance or compensate the action of the estrogens. The article is illustrated with many tables and the bibliography contains 42 references.

RICARDO L. GORBEA

Gynecology

McKay, Donald G., Street, Russell B., Jr., Benirschke, Kurt, and Duncan, Christopher J.: Eosinophilic Granuloma of the Vulva, Surg., Gynec. & Obst. 96: 437, 1953.

Detailed reports are given on the clinical findings and course of 3 cases of eosinophilic granuloma of the vulva. Included are photomicrographs and clear descriptions of the gross and microscopic findings. Microscopic examination of biopsied material shows an infiltrate characterized by an irregular accumulation of large histiocytes with indented, irregular nuclei, and pink, granular cytoplasm. Between the cells are scattered eosinophils, polymorphonuclear leukocytes, and lymphocytes.

Predominant symptoms in these cases were those of diabetes insipidus, menstrual dysfunctions, and the development of cutaneous, subcutaneous, osseous, oral, and vulvar lesions. When the disease produces localized masses in the skin, they tend to occur around body orifices. The vulvar lesions are often symmetrical and tend to be eczematous and exudative in children, while in adults they tend to be yellow-brown tumors.

Brief descriptions of eosinophilic granuloma of skin and bone, Hand-Schüller-Christian disease, and Letterer-Siwe disease are given. The authors believe that the histologic and clinical evidence indicates that all of these conditions are really different expressions of the same basic disease process.

Therapy is inadequate but roentgen treatment or local excision may yield good palliation.

ROBERT B. WILSON

Barns, Tom, and Snaith, Linton M.: Tuberculous Cervicitis; A Report on Two Cases and a Note Upon the Natural History of the Condition, J. Obst. & Gynaec. Brit. Emp. 60: 131, 1953.

Two cases of tuberculous cervicitis are described. The first occurred in a 15-year-old patient who had a premature labor following an antepartum hemorrhage at 30 weeks' gestation. Pulmonary tuberculosis was unrecognized in her antepartum course but subsequently serial x-rays were regarded as evidence that a very early tuberculous lesion of the lung developed during pregnancy. Six weeks post partum a persistent low-grade fever was observed and examination revealed a right-sided tubal mass. Diagnostic curettage and cervical biopsy revealed typical miliary tuberculosis in the endometrium and cervix and on bacteriological examination tubercle bacilli were recovered from the endometrium.

The second patient was a 25-year-old woman who developed a pleural effusion at 24 years of age. During the time of the pleural effusion, the patient's menses underwent striking alterations from a 28 day cycle lasting 6 days to a 35 day cycle lasting 11 days. Pelvic examination revealed a florid, proliferative mass growing from the cervix, which bled readily and was hard, irregular, and painless. Dilatation and curettage and cervical biopsy revealed tuberculous endometritis and cervicitis.

The authors believe that female genital tuberculosis develops during the phase of bacteremia which is known to occur during and for a short time after the development of the primary tuberculous focus. They state that owing to the rarity with which the primary infection occurs after the age of 20, it would appear that genital tuberculosis is essentially a disease of adolescence, however long it may remain latent before discovery in later life.

GEORGE SCHAEFER

Gynecologic Operations

deMorales, Arnaldo: Indications for Total Hysterectomy in Nonmalignant Conditions of the Uterus, Arq. de clin. ginec. 4: 11, 1951.

After reviewing the literature of the last decade where the indications for total hysterectomy in nonmalignant conditions of the uterus are discussed, and the advantages of total over subtotal hysterectomy in these cases are emphasized, the author quotes the statistics reported by the different clinics on the incidence of cancer of the cervical stump and the results of vaginal and abdominal total hysterectomy.

Reporting on his experiences in Brazil where he has, for a long time, advocated total hysterectomy in the treatment of nonmalignant conditions of the uterus in women at the menopause or postmenopausal period, primarily for the prevention of cancer, he cites the figures obtained in his gynecological clinic where a conservative policy for the younger group of women is followed, although total hysterectomy is usually indicated for the older ones. Twelve cases of cancer of the cervical stump, after subtotal hysterectomy, were observed in his clinic.

It is obvious that no procedure in any clinic may be considered as a constant routine. There are indications for vaginal hysterectomy as well as for abdominal hysterectomy. Total hysterectomy, in the latter cases, should be the method of choice, since it excludes the danger of an infected or cancerous cervix.

Total hysterectomy has advantages which advocate its use in the majority of cases. The author feels satisfied, therefore, that in the light of our present knowledge the present trend toward total hysterectomy in nonmalignant conditions of the uterus shows a continuing aim to benefit and protect our patients against cancer.

RICARDO L. GORBEA

Ramirez, D.: Vaginal Atresia: Its Treatment by the Use of Heteroplastic Homologous Transplant, Personal Technique of the Author, Ginec. y obst. de México 8: 22, 1953.

The author introduces his paper with a résumé of embryologic considerations and historical data on vaginal atresia. He then presents the case of a 24-year-old white woman, married, with vaginal agenesia. There were no anomalies found in the urinary tract. Following the author's personal and original technique, a vagina was built using homologous tissue transplants from another woman who was operated upon 20 minutes before for second-degree uterine prolapse. Blood groups and Rh factors were similar in both patients. The patient was hospitalized 19 days, and within 45 days was able to have sexual intercourse. Six months later the vagina was 7 cm. in depth. The grafted tissues were cytologically studied then and it was found that both the basal and stratified layers retained their normal characteristics. Within a year the patient was able to attain perfect sexual libido. It is the opinion of the author that the success of this operation was due to the fact that both patients had similar blood and Rh groups, both had good ovarian function, and postoperatively antibiotics and estrogens were used for two weeks. The author has inserted numerous diagrams and roentgenograms to illustrate his technique. The bibliography contains 28 references.

RICARDO L. GORBEA

Cuaresma Gutierrez, C.: Prevention of Bladder Dysfunction Following the Wertheim Operation, Ginec. y obst. de México 8: 36, 1953.

The author reports on the frequent postoperative complication of primary retention followed by incontinence after a radical Wertheim hysterectomy. He feels that this is due to partial parasympathetic denervation of the bladder brought about by the operative procedure, together with mechanical extirpation of most of the bladder supports. The author has followed a postoperative as well as operative finale which has helped prevent these complications. He diminishes the bladder capacity by applying 3 concentric purse-string sutures in the posterior denuded portion of the bladder which has been left without any support. He peritonizes this portion with the vesicouterine fold and also covers the raw area anterior to the rectum, thus forming a cul-de-sac of Douglas similar to that of the male. He leaves a retention catheter of four to eight days and follows this with injection of 30 c.c. of Mercurochrome to stimulate vesical contractility. Early ambulation is enforced and the use of antibiotics is carried on until there is no evidence of infection.

RICARDO L. GORBEA

Labor, Management

Gibson, George B.: Surgical Induction of Labour, J. Obst. & Gynaec. Brit. Emp. 59: Dec., 1952.

Presented are the results of 843 consecutive cases occurring from 1946 to 1950, in which surgical induction of labor was performed, an incidence of 9.9 per cent. In the series, 468 were primigravidas and the average age was 29½ years. A review of the indications reveals that 833 had a definite complication, with pre-eclampsia occurring in 635, accidental hemorrhage in 61, hydramnios in 28, placenta previa in 27, intrauterine death in 19, erythroblastosis in 19, etc. Only 10 were performed for convenience, in contrast to American

practice, where induction for the convenience of the patient and obstetrician occurs frequently. (Plass and Seibert, 1936, and Keettel, Diddle, and Plass, 1940, reported large series.)

Guttmacher and Douglas (1931) stressed the importance of cervical ripeness in relation to the success of surgical induction of labor, which criterion was present in 80 per cent of Gibson's series.

The methods of induction consisted almost completely of rupture of the membranes (forewaters in 529, hindwaters in 202) and the insertion of a bougie or stomach tube into the lower uterine segment. Rupture of the hindwaters was frequent early in the series, but as the latent interval tended to be prolonged, the method became less popular. In the whole series, the latent period was less than 24 hours in 70.8 per cent of the cases. Whereas the period in primigravidas had a consistent relationship to the state of the cervix, this was not true in multigravidas.

Practically all of the inductions were performed under cyclopropane, oxygen anesthesia, using aseptic precautions. After rupture of the membranes, the patient was given Pitocin (2 units) intramuscularly at hourly intervals for 1 to 3 hours the onset of contractions being a contraindication to further injections. If the cervix was unripe, a bougie or stomach tube was favored. If labor had not commenced 48 hours later the tube was removed and the forewaters were ruptured.

The average duration of labor in primigravidas, after rupture of the membranes, was 16 hours, but 1 in 5 had a labor lasting more than 24 hours. There were 590 normal deliveries, 176 forceps deliveries, 87 breech deliveries, and 34 cesarean sections.

In the series, 7 per cent had a definite pyrexia. Infection was uncommon after rupture of the membranes but frequent when other methods were employed. Prolapse of the cord occurred only once following rupture of the membranes, whereas it was noted 4 times after bougie introduction.

There were 5 maternal deaths, an incidence of 0.59 per cent (three could not be attributed to the induction). Of the remaining two (both followed bougie introduction) one was directly attributable to induction and the other probably was, the first being due to a rupture of the uterus and the other suggestive of a fulminating puerperal sepsis.

The corrected fetal mortality was 11.9 per cent, among which prematurity was a frequent finding (23 fetuses weighed less than 3 pounds).

In his discussion, the author concludes that when the cervix is ripe, rupture of the membranes provides a satisfactory imitation of the natural onset of labor and no other method of induction need be considered. If the cervix is unripe he concludes that the uterus is not primed for the onset of labor and is loath to respond to the stimulus provided by any method of induction. A prolonged latent period following rupture of the membranes did not lead to sepsis, if vaginal examinations were avoided. However, intrauterine death occurred in 25 per cent of the cases in which the latent period exceeded 72 hours, which was thought due probably to placental insufficiency. Bougie introduction resulted in two maternal deaths and sepsis was common, indicating that this method should be discontinued. Elective cesarean section is not advised unless a valid indication exists. It is felt that rupture of the membranes has not proved a serious maternal risk and should be tried first as a considerable number of promising cases will start into labor and cause no anxiety, thereby avoiding unnecessary section. If labor does not commence in 72 hours, the case should be re-evaluated.

ELMER E. KRAMER

Amigo De Bonet, N.: Internal Version: Techniques and Personal Experiences, Toko-Ginec. práct. 11: 533, 1952.

This is a historical statistical and technical report on 287 internal versions performed by the author without a maternal mortality at the Clinica de la Residencia Maternal in Barcelona. The author is a staunch follower of this procedure and many times uses it in

conjunction with symphysiotomy rather than resort to abdominal delivery by cesarean section, contrary to the American school of thought. There was fetal mortality in four cases of his series.

The author reports on the techniques of the Potters and Rojas and combines these and his own to turn and extract the fetus. He prefers this method of delivery to cephalic extraction with forceps, because he believes the latter method is responsible for many cases of strabismus, epilepsy, and mental derangements, the trauma with the forceps being responsible for these conditions. The text contains a number of bibliographical references.

RICARDO L. GORBEA

Mammary Glands

Neuweiler, W., and Kästli, P.: The Value of Aureomycin in Puerperal Mastitis, Gynaecologia 135: 1, 1953.

Penicillin and some other antibiotics are of no value in the treatment of some forms of puerperal mastitis. Therefore, the value of oral aureomycin was studied, first, to see if it was secreted in the milk in an active form, and, second, as a clinical therapeutic test for antibiotic efficacy. The procedure for testing this was as follows: Aureomycin in sufficient quantities (usually 1.0 to 1.5 Gm. daily) was given to lactating women. The expressed milk was tested against known cultures of various organisms in Petri dishes. The test organisms used were *Streptococcus lactis; Streptococcus agalactiae,* and *Staphylococcus aureus.* Known strains of these organisms were grown on culture media. In the center of each plate a measured quantity of the milk to be tested was placed and the antibiotic effect determined by the extent of the sterile area surrounding the milk droplets. By means of this in vitro experimentation, it was definitely felt that not only is aureomycin secreted in the milk, but also it is secreted in large enough quantities to have a definite therapeutic effect, at least against the organisms tested. It was therefore concluded that aureomycin, when given in adequate dosage, by mouth, was a most suitable antibiotic agent in the treatment and cure of puerperal mastitis.

L. B. WINKELSTEIN

Menstruation, Dysmenorrhea

Manzur, C., and Ortega, E.: Primary Dysmenorrhea, Ginec. y obst. de México 7: 437, 1952.

The authors review the literature on primary dysmenorrhea and arrive at certain definite conclusions concerning the etiology, symptomatology, diagnosis, and treatment of this condition. For one thing, the etiology is still unknown. It occurs mostly in young women, predominantly in virgins, and rarely in those who have become pregnant. Primary dysmenorrhea is usually associated with the process of ovulation. A low pain threshold is always present in women with primary dysmenorrhea. It is believed that angiospasm of the endometrial arteries is responsible for the pain, but this, again, has not been proved. Hygienic, medical, and surgical treatments are outlined, but of these the only lasting treatments are presacral neurectomy and the injection of the ganglion of Frankenhäuser with 85 per cent alcohol. Stem pessaries and simple dilatation of the cervix occasionally give lasting cures. Estrogens and androgens are the only hormones capable of temporarily controlling the pain by suppressing ovulation. There is a bibliography with 36 references.

RICARDO L. GORBEA

Pregnancy, Complications

Laforet, C.: Etiology of Placenta Previa, Geburtsh. u. Frauenh. 13: 150, 1953.

Despite all advances made in the etiology, diagnosis, and treatment of obstetrical complications, the cause of the development of placenta previa still remains unknown.

However, with the advent of antibiotic therapy and the more liberal and safer use of whole blood transfusions, the mortality of mothers and babies from this cause has steadily decreased because of the steady increase in the use of cesarean section. On the basis of her observations of many cases of placenta previa in comparison with normal deliveries, the author feels that the cause of this obstetrical calamity is twofold. In the first of these causes, it was noted that the placentas in total and partial previa were actually larger than normally situated placentas, and thus on a purely mechanical basis had a tendency to occupy more of the interior of the uterine cavity, and statistically to involve more of the lower segment. This observation was made on the measurement of the diameters of normally and abnormally implanted placentas. It was found that whereas the average diameter of the placenta with normal high implantation (200 cases) was 311 cm., in cases where low implantation or marginal implantation occurred, the diameter of the placenta was 355 cm. (50 cases), and in true complete placenta previa the diameter averaged 586 cm. (40 cases). This variation in size, the author feels, is probably due to some developmental anomaly of the egg itself (since abnormal fetuses are found more commonly with placenta previa) or to some factor in the endometrium which does not allow for proper nidation at the top or in the upper third of the uterine cavity.

The second cause of placenta previa is thought by the author to be due to nidation occurring on the anterior wall of the uterus, rather than on the posterior or lateral wall. On the basis of the examination of the placental site in 40 cases of true placenta previa, which were treated personally by cesarean section by the author, anterior insertion was noted in over 60 per cent of the cases, whereas in normal cases less than 30 per cent were thus situated. The author feels that the explanation for this lies in the fact that the anterior wall of the uterus has more active peristalsis than the remainder of the uterus, and has the tendency to force implantation at a lower level or in the lower segment of the uterus.

L. B. WINKELSTEIN

Kremling, H.: Urinary Calculi and Pregnancy, Geburtsh. u. Frauenh. 13: 145, 1953.

Kidney or ureteral stones which develop or become symptomatic during pregnancy pose problems which are greater both diagnostically and therapeutically than kidney or ureteral stones occurring during the nonpregnant state. It has been rationalizd that, because of the impingement of the gravid uterus against the ureter at the pelvic brim, a urinary stasis develops which predisposes to the development and growth of gravel. However, on a statistical basis this has not proved true, since the effect of such impingement is balanced by hypertrophy and growth of the ureteral musculature and the formation of a physiological hydroureter.

The main symptoms and findings of kidney or ureteral stone are: (1) dysuria; (2) polyuria; (3) ureteral colic; and (4) hematuria in a catheterized specimen. Diagnosis may be made or confirmed on these symptoms or findings plus the findings on intravenous pyelography, cystoscopy, or ureteroscopy. It was noted that stones in the urinary tract during gestation may vary from those of microscopic size to concretions the size of a walnut. The symptomatology is not increased by the size of the stone, since very small ones may produce greater discomfort than may very large ones.

Management of urinary tract calculi during pregnancy should be conservative unless evidences of kidney infection or kidney function involvement are noted. Conservative therapy consisted of physiological ureteral dilators, postural exercises, and administration of prophylactic antibiotics for the prevention of infection. If infection does occur, or if evidences of loss of kidney function develop, as evidenced by spiking temperatures, chills, toxemia, and changes in the urinary values and output, surgery is the method of choice and should be undertaken before permanent kidney damage is present. When conservative measures fail, pyelotomy is the surgery of choice. The author feels, however, that although surgery must be eventually undertaken, it is safer and will result in less debilitation if done after, rather than before, delivery.

When the calculus is in the ureter itself, drugs which relax and dilate the ureter should be tried first. This failing, ureteroscopy with the view of fracturing and delivering the concretion may be attempted. Ureterotomy is a dangerous procedure and mechanically difficult during pregnancy and should be utilized only as the last resort. When the ureteral stone is passed into the bladder, the problem is controlled.

Prophylaxis of urinary concretions is not known. It is felt that the urine should be as dilute as possible, which can be accomplished by the imbibition of large quantities of liquids, especially acid liquids. Substances such as the sulfonamides and others known to precipitate crystals in the urine should be avoided. Postural exercises thought by some to have value do not appear to be worth a great deal. In general the prophylaxis consists of large fluid intake, to prevent the precipitation of oxalates, phosphates, and urates which might act as a nucleus for the formation of stones.

L. B. WINKELSTEIN

Chesley, Leon C.: Eclampsia at the Margaret Hague Maternity Hospital, Bull. Margaret Hague Maternity Hosp. 6: March, 1953.

This paper presents an analysis of the cases of eclampsia which occurred in the Margaret Hague Hospital from the time of its opening to Dec. 31, 1951. There was a total of 135,973 deliveries during this period with 303 eclamptics, an incidence of 0.22 per cent. There were 30 maternal deaths, a mortality of 10 per cent, and a gross fetal mortality in these women of 30.6 per cent.

In this series there occurred 122 examples of antepartum eclampsia, with a mortality of 14.1 per cent; 92 intrapartum with a mortality of 4.4 per cent; and 86 postpartum with a mortality of 7 per cent.

Cerebral hemorrhage was an important factor, noted in 43 per cent of the fatal cases.

The methods of therapy are not presented.

The author presents an interesting discussion of several doubtful and borderline cases. A steady and progressive decrease in the incidence of eclampsia in the period studied is noted, doubtless the result of improved prenatal care and the detection of pre-eclamptic signs at an earlier period. There were 3 examples of nonconvulsive eclampsia in the series. One example of eclampsia in association with hydatid mole was observed.

KARL M. WILSON

Morris, Norman: Hexamethonium Compounds in the Treatment of Pre-eclampsia and Essential Hypertension During Pregnancy, Lancet 1: Feb. 14, 1953.

The author reports his findings in 10 cases of pregnancy complicated by pre-eclampsia and essential hypertension. Only those cases in which the fetal prognosis was poor and which had failed to respond to other methods were treated with hexamethonium compounds. The author advises against the oral administration of such drugs because of the unpredictable responses; he feels that even transient periods of hypotension may produce fatal changes in the uteroplacental circulation. Parenteral administration must be carefully controlled. Resistance to the drug occurs within a few days; he suggests that although the autonomic blockade was still in force (pupillary paralysis), the hypertension was sustained by the increased action of a humoral pressor mechanism. The blood pressure generally was lowered, but the author does not believe the course of the disease was appreciably altered. There were no effects on labor, and no important maternal side effects. The author points out that the drugs are present in high concentrations in the amniotic fluid and believes it arrives there from the fetal urine. The high concentrations of the drugs in the amniotic fluid with reabsorption by the fetus from swallowed fluid may predispose to the occurrence of paralytic ileus which did occur in 2 of the 10 fetuses. The author concludes the drugs should be used only when conventional therapeutic measures have failed.

DONALD G. JOHNSON

Puerperium

Hemphill, R. E.: Puerperal Mental Illness, Brit. M. J. 2: Dec. 6, 1952.

The editorial is concerned with the article by Dr. R. E. Hemphill in the Dec. 6, 1952, issue of the *British Medical Journal* on a study of puerperal mental illness. The incidence makes this a complication of pregnancy of considerable importance. The editorial indicates the room for improvement in preventing confusional states or toxic delirium, and that these conditions should be treated in a special unit of a lying-in hospital since they are organic and not affective or schizophrenic reactions. The importance of early recognition is emphasized. Two findings of Hemphill's report are of special interest: first, the occurrence of depressive states which resemble the involutional states of later life; and, second, the poor prognosis for schizophrenic patients. If puerperal schizophrenia follows a course different from other forms of the disease, then it should be considered an entity by itself and further investigation into its pathogenesis is of utmost importance.

DONALD G. JOHNSON

Hemphill, R. E.: Incidence and Nature of Puerperal Psychiatric Illness, Brit. M. J. 1: Dec. 6, 1952.

The author has reported on a study of case records of patients delivered at maternity hospitals in Bristol to determine the importance of physical and psychological factors in the development of mental disease. All cases of mental illness related to pregnancy or the puerperium admitted to mental hospitals during the same 10 year period were studied. Only the cases with considerable mental unbalance were included in the study. The incidence of mental reactions in the maternity hospital cases was 1.7 per 1,000, of which 1 per 1,000 was admitted to mental hospitals. The incidence of mental illness in the total number of delivered patients was 1.4 per 1,000. The cases were classified ultimately into affective (including manic-depressive cases and puerperal depression), schizophrenic (including mixed schizophrenic cases), and other cases (including neurosis, confusion and exhaustion, toxic delirium, etc.). With respect to etiological factors, 13 per cent had a history of previous mental illness; there was a positive family history in 14.5 per cent of all cases, but in 25 per cent of the schizophrenic group. There was no evidence that parity, age, multiple births, physical illnesses, or psychological factors played any role in the etiology of mental illness. The personalities of those suffering from puerperal depression and mixed schizophrenic reactions were characterized as dependent, overanxious, obsessional, and rigid in type. Delirium and reactions to exhaustion and toxemia as well as manic-depressive episodes do not differ from those not related to pregnancy. The author believes that there is a psychiatric entity called puerperal depression which differs from manic-depressive psychosis, but resembles involutional melancholia. It makes its appearance within the first two weeks post partum; it is extremely intractable even when treated by convulsive therapy. Eventual recovery or spontaneous remission is usual. The prognosis in schizophrenia was practically hopeless. The author suggests that the sudden deprivation of the placenta and its normal hormone content produces a disturbance in the endocrine equilibrium which, working on a predisposed constitution, produces the mental illness. The author believes that therapeutic interruption of pregnancy should be seriously considered if less than a year has elapsed since recovery from a puerperal psychosis which ran a prolonged course, if there is a bad family history of mental illness, and if there is a history of more than one attack of puerperal psychosis. He feels that it is very dangerous to allow a patient having recovered from puerperal schizophrenia to become pregnant again. The author believes that good antenatal care may do much to reduce psychoneurotic and mild nervous reactions, but that nothing can be done to prevent puerperal depression or puerperal schizophrenia.

DONALD G. JOHNSON

Sterility

Campos da Paz, A.: Partial Tubal Blockade, Rev. brasil. de cir. 24: 407, 1952.

The presence of adhesions in the space between the surface of the ovary and the tubal ampulla, the fimbriae, is here described by the author as a possible cause of sterility in an apparently normal couple. It seems that this particular space has not been given the attention and consideration which it should have. The author reviews a series of 500 cases of sterility in which partial tubal blockade occurred in 7.2 per cent of the cases. This was determined by the use of hysterosalpingography and tubal insufflation with gas, procedures which the author advises should be used routinely during the investigation of a sterile couple. The author divides the treatment of this condition into medical and surgical categories, always remembering that any surgical procedure used to remove the adhesions present may stimulate the formation of new adhesions. The medical treatment, which should precede the surgical, is directed toward eliminating the inflammatory process responsible for the condition. This is attempted by the use of antibiotics, diathermy, etc. If any surgical procedure is used, it should be a most delicate and nonirritating one. At best the results are poor as the condition, adhesions, is bound to recur.

RICARDO L. GORBEA

Editorial on Oral Contraception: Lancet, Nov. 22, 1952.

The Lancet, in its issue of Nov. 22, 1952, editorializes on the subject of "Oral Contraception." The editor quotes from the presidential address of Prof. A. V. Hill, F.R.S., before the British Association on the ethical dilemma for preventive medicine in the prospect that "the pressure of increasing population uncontrolled by disease would lead not only to widespread exhaustion of the soil and of other capital resources but also to continuing and increasing international tension and disorder, making it hard for civilization to survive."

He then summarizes the work done in the past on hyaluronidase and phosphorylated hesperidin and reports on the paper of B. F. Sieve in Science on the results of giving phosphorylated hesperidin as an oral contraceptive to 300 couples. As with other comments on Sieve's work, Lancet feels his results of 298 successes is almost too good to be true. The article ends with a plea for confirmation of this work in the hope that a simple and safe oral contraceptive may be found so that women all over the world might exercise some rational control on the number of their children.

CHARLES M. MCLANE

Guerrero, C. D., and Lopez Satibanez, L. M.: Etiopathogenesis, Classification, and Exploration of Sterility of Cervical Origin, Estudios sobre esterilidad 3: 165, 1952.

The author gives us a résumé of all possible causes of sterility of cervical origin with pertinent discussion of each, followed by a list of seven ideal conditions of the cervix necessary for eventual fertility. These are: (1) anatomically well developed, (2) normally situated, (3) unobstructed external os, (4) permeable canal, (5) even caliber throughout, (6) lined with normal mucosa, (7) capable of cyclical production of mucus. The modification or absence of any of these factors predisposes to sterility of cervical origin.

The author then outlines the methods which he advocates and the factors he takes into account in exploring the cervix for diagnosis: (1) palpation and speculum examination, (2) cytologic, bacterioscopic, and culture studies, (3) permeability and axis of cervical canal, (4) rigidity of cervix, (5) flaccidity of the canal under manometric pressure, (6) shape of the cervical canal, (7) hysterography, (8) fluidity of the cervical mucous plug, (9) pH of cervical mucus, (10) mucus "fern" test, formation of fernlike pattern denoting normal status, (11) Huhner test, and (12) the endocervical biopsy.

RICARDO L. GORBEA

Correspondence

Diabetes in Pregnancy: Marked Differences in Results

To the Editors:

I have just read with interest the article by Dr. Walter S. Jones on "Diabetes in Pregnancy," published in the August issue of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY. I am enclosing a reprint on this subject, titled "Pregnancy Complicated by Diabetes Mellitus," published in February, 1953, in *Obstetrics and Gynecology.* I realize this paper was not available at the time Dr. Jones' article was accepted for publication.

I am unable to tell from Dr. Jones' article the severity classification of his patients, which I believe to be a most important part of the picture. Seventy-one and eight-tenths per cent of our patients are classified as having severe diabetes, based on age at onset, duration of the disease, and the presence of vascular damage (Classes C, D, E, and F). This type of gradation aids greatly in the prognosis and treatment and is of particular value in the early timing of delivery. We now have a classification for other medical complications, such as heart disease and toxemia; why not diabetes? The prognosis of the pregnant woman with diabetes of short duration, or one who developed diabetes during pregnancy, should not be compared in any way with that of a juvenile diabetic, one with the disease of 20 years' duration, or one with vascular damage. Dr. Jones' gross fetal mortality of 29.6 per cent without hormonal therapy corresponds favorably with that given in articles by Reis, Given, Hurwitz, and others. Dr. Jones suggested that by better prenatal care, with emphasis on the prevention of toxemia, the fetal mortality should be lowered to 10 per cent. We were able to produce a 90 per cent fetal survival rate in a group of 128 viable pregnancies, 71.8 per cent of the cases of diabetes being classified as severe (Classes C, D, E, F). We feel this was accomplished by good medical control, careful prenatal care, hormonal therapy, and early timing of delivery. I feel sure Dr. Jones and the authors of other articles have been careful to control the diabetes medically and have given close and meticulous prenatal care. This would then suggest that a fetal mortality of 10 per cent was in part accomplished by hormonal therapy and early timing of delivery. There is no question that the stillbirth rate is lowered in the patient with advanced and severe diabetes by early delivery between the thirty-fourth and thirty-seventh weeks of gestation.

There is some evidence that hormonal therapy reduces the incidence of pre-eclampsia in the nondiabetic patient, and this is further emphasized since our toxemia rate was only 5 per cent. Toxemia of pregnancy, superimposed upon diabetes, greatly increases the fetal mortality. I agree that hormonal therapy is an added expense and an increased inconvenience but if it will in part reduce the toxemia rate it is well worth these disadvantages.

If everyone interested in diabetes in pregnancy would adopt these classifications previously presented by Dr. Priscilla White, we would all have a clear idea of the type of diabetic patient being studied. Someone reporting a group with severe diabetes without hormonal therapy and a fetal mortality of 10 per cent will aid greatly in clearing up the need for hormonal therapy.

H. BRISTOL NELSON, M.D.
CHIEF, OBSTETRICS-GYNECOLOGY DEPARTMENT

PERMANENTE MEDICAL OFFICES
515 MARKET STREET
SAN FRANCISCO 5, CALIF.
AUG. 20, 1953

Reply by Dr. Jones

To the Editors:

I heard Dr. Gillespie read the article on "Pregnancy Complicated by Diabetes Mellitus," by Drs. Nelson, Gillespie, and Priscilla White, at the meeting of the American Academy, and studied it with interest when it was published. The current controversy between the "hormone" and "nonhormone" schools of thought waxes hot, but there is no place in it for acrimony. When the smoke has cleared away I am sure we will all have settled on some common ground of policy.

Dr. Nelson's letter brought up a number of points, which are most easily discussed under separate headings:

1. Difference in Type of Material.—Without doubt we are talking about two series which vary considerably in character of patients. Because of the prestige of Dr. White and the Joslin Clinic, he had a phenomenally high proportion of cases of the worst kind of diabetes, as evidenced by approximately 50 per cent being in Classes D, E, and F. On the other hand, our series was a catchall assortment, some of it having been poorly handled in one way or another, with 15 per cent in Class D and few if any in Classes E and F. The other reports from obstetrical clinics, quoted by him, are closely comparable with ours in composition. I tried to make this difference in type of material clear in my paper. I also demonstrated that two-thirds of our 29.6 per cent fetal loss should have been preventable. This is a matter of basic good medical and obstetrical management, and has nothing to do with whether or not the patient received hormonal therapy.

2. Hormone Therapy.—I have no objection to hormone therapy, provided it is properly carried out, and in the right type of case. Several of my private patients have been so treated. Results like Dr. Nelson's, in the category of diabetic patients he is handling, must give pause to even the most ardent "nonhormone" advocate.

As stated in the introduction, my paper aimed at establishing some sort of base line for obstetrical results, which could be used for comparison with those of other studies. The conclusion was that the fetal loss, in a clientele representing a fair cross section of the general population, should not much exceed 10 per cent.

When I started this study, my thinking was influenced by what was happening in this community and all over New England, following Dr. White's report of 1947. Neither the obstetricians nor the internists had been very happy with their results in diabetes. The introduction of hormones seemed to offer an easy solution. The method became fashionable because it was the newest thing on the market. Many women received it whom I am sure Dr. Nelson would not have so treated. Those with relatively mild cases, who had suffered previous disasters due to inferior medical or obstetrical care, were put on hormones. All concerned were on their toes from the start. Then the good outcome was credited to the hormones, although it was often obviously attributable to the improved all-round management. In some instances one could detect a tendency to let the hormones do the job, while the physicians rested on their oars. Such a psychology could do nothing but increase the fetal loss.

My paper was directed, not at experienced specialists in the field like Dr. Nelson, but at the average obstetrician who may see one diabetic patient in three or four years. Among the points made were that: (a) The primary responsibility is medical and obstetrical. Hormone therapy in selected cases (such as his must be) is strictly an adjunct. (b) Indiscriminate hormone therapy, in Class A and many of what he calls Class B women, is a waste of effort and money.

This seems to voice the current trend of obstetrical thinking. In Chicago, Dr. Gillespie and several of the gentlemen from Dr. Reis' clinic debated Dr. Nelson's paper rather heatedly. Dr. Randall, the moderator, concluded the session with the remark that he was no longer using hormones. I discussed diabetes on a panel at the 1952 fall meeting of the New England Obstetrical and Gynecological Society. With the exception of the group from the

Boston Lying-in Hospital, there was a notable lack of enthusiasm for hormones among the men who handle the diabetic patients at the other large Boston hospitals. It is fair to assume that this is because the general run of material in obstetrical clinics is comparable to ours in the proportion of relatively mild cases.

3. Toxemia.—Space does not permit a lengthy discussion of whether stilbestrol prevents pre-eclampsia in the normal patient. Frankly, I do not believe that it does. The original work of the Smiths has never been satisfactorily substantiated. I know of no large clinic which is now using this method of toxemia control. I have abandoned its use in my private patients who had previous toxemia; and we are not using it in our Toxemia Clinic. Likewise, I am very skeptical that stilbestrol, or other hormone therapy, will appreciably reduce the incidence of pre-eclampsia in the diabetic patient.

4. Early Delivery.—There is no need to go into this here., I discussed my feelings on the subject, and the reasons for them, at length in the paper.

5. Severity of Diabetes.—Now to come to the main question in Dr. Nelson's letter. We have generally followed the severity classification made by the internists. This is based primarily on the insulin requirement, with consideration given to such factors as the "brittleness" of the diabetes, retinal changes, etc. Under this system we had 103 mild and 59 severe cases (Table IV, page 325). The fetal loss was:

	NUMBER OF CASES		FETAL LOSS IN GROUP		PROPORTION OF TOTAL FETAL LOSS	
Mild	103/162	73.6%	28/103	27.2%	28/48	58.3%
Severe	59/162	36.4%	20/59	34.0%	20/48	41.7%

It is not possible to group these patients accurately into the grades suggested by White, for several reasons. Prior to 1947 there were no routine roentgen study of the vascular tree, detailed retinal studies, etc. Our x-ray equipment was installed in 1936, and most of the available plates are naturally pelvimetries. I have reviewed those which have not been destroyed for storage reasons; and can say that none of them show sclerosis of the pelvic vessels. In the early years of the series, many cases lack description of the retina. Within these limits of the available information, the following is a rough breakdown under Dr. Nelson's system of classification:

CLASS	CASES		FETAL LOSS	
A	35	21.6%	5/35	14.3%
B	75	46.2%	22/75	29.3%
C	28	17.2%	10/28	35.7%
D	24	15.0%	11/24	45.8%
E	(None. If more x-ray evidence were available, a few of the Class D cases might be promoted to Class E)			
F	Definitely none			

6. Classification of Severity.—I heartily agree with Dr. Nelson that we need an acceptable classification which can be used by all writers. White's system is a good starter, but I see two objections to it:

(a) One is a minor matter of practice, especially in the smaller centers. It can be anticipated that many cases will lack the x-ray studies necessary to distribute them accurately between Classes D and E.

(b) The principal objection is that White's classification is based solely on the age at onset, duration of the diabetes, and such objective criteria as sclerosis, etc. It does not take into consideration what might be called the subjective clinical severity, the insulin requirement of the patient. For example, a large number of the cases we called severe fell into Dr. Nelson's Classes B and C, and they provided a substantial proportion of the fetal loss in these groups. Paradoxically there were three times as many clinically severe cases in Class C as in Class D, with three times as great a fetal loss. Conversely, there were a few women placed in Class D, because of long-standing diabetes or established hypertension, whose cases were clinically so mild as to require very little insulin; and they contributed no fetal loss.

DR. NELSON'S CLASS	PATIENTS WE CALLED CLINICALLY SEVERE		FETAL LOSS THESE PATIENTS CONTRIBUTED FOR THE CLASS	
A	0/35	0.0		0.0
B	29/75	38.7%	8/22	35.5%
C	24/28	85.8%	9/10	90.0%
D	6/24	25.0%	3/11	27.3%

Any classification that is finally agreed upon will have to take this factor of the insulin requirement into consideration.

7. Proposed Classification.—The classification of heart disease in pregnancy originated with the medical men. The American Committee on Maternal Welfare assumed the responsibility for the toxemia classification, because of the death rate involved. That body may not care to sponsor a classification for a disease such as diabetes, which today carries a minimal maternal risk. Perhaps it might be undertaken as a function of the American Academy of Obstetrics, with interested internists and obstetricians both represented on the subcommitteee.

WALTER S. JONES, M.D.

PROVIDENCE LYING-IN HOSPITAL
PROVIDENCE, R. I.
SEPT. 21, 1953

Items

The American Board of Obstetrics and Gynecology

The next scheduled examination (Part I), written examination and review of case histories, for all candidates will be held in various cities of the United States, Canada, and military centers outside the continental United States, on Friday, Feb. 5, 1954.

Case abstracts are to be sent by the candidate to the Secretary as soon as possible after receiving notification of eligibility to the Part I written examination.

Candidates are reminded at this time that Application for re-examination in Part II must be made by the candidate prior to February 1 of any year.

ROBERT L. FAULKNER, M.D., SECRETARY
2105 ADELBERT ROAD
CLEVELAND 6, OHIO

The Founding of the Arkansas Obstetrical and Gynecological Society

With this number of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, the Arkansas Obstetrical and Gynecological Society becomes one of the JOURNAL'S supporting Societies. The new Society was founded on April 22, 1953. The founding officers were Dr. Eugene T. Ellison, Texarkana, Arkansas, as President; Dr. Willis E. Brown, Professor and Head of the Department of Obstetrics and Gynecology at the University of Arkansas School of Medicine, President-elect, and serving in the capacity of vice-president; Dr. Robert W. Ross, 908 Donaghey Building, Little Rock, Ark., Secretary and Treasurer. The new Society meets twice yearly. The first meeting was held in the fall of 1953 and the second meeting will be held in the spring in conjunction with the Annual Meeting of the Arkansas State Medical Society.

John Warton Harris Obstetrical Society

The John Warton Harris Obstetrical Society was organized on Sept. 5 and 6, 1953, by former residents of Dr. John W. Harris, Professor of Obstetrics and Gynecology, the University of Wisconsin Medical School, and Chairman of the Department of Obstetrics and Gynecology, State of Wisconsin General Hospital, Madison, Wis. The Society was founded in honor of Dr. Harris as teacher and friend, with membership limited to residents trained by Dr. Harris and members of his department.

The following officers were elected: President, Madeline J. Thornton, President-elect, E. Russell Muntz, Secretary-Treasurer, Alice D. Watts.

Assises Françaises de Gynécologie de 1954

Because of material difficulties, the Assises Françaises de Gynécologie, which was to take place at Dijon, will be held in Paris, July 22 to 24, 1954.

The subject will be "The Treatment of Genital Prolapse."

President, Claude Béclere. Reporter General, Raoul Palmer.

For information and registration, write to the Secretary General, Robert Sénéchal, 31 Rue Raynouard, Paris 16e.

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January and July)

American Academy of Obstetrics and Gynecology. (1945) *President,* Bayard Carter. *Secretary,* C. Paul Hodgkinson, 116 S. Michigan Ave., Chicago 3, Ill. Next meeting, Palmer House, Chicago, Dec. 13-17, 1954.

American Gynecological Society. (1876) *President,* Richard W. Te Linde, Baltimore. *Secretary,* John I. Brewer, 104 S. Michigan Ave., Chicago 3, Ill. Annual meeting at Hot Springs, Va., May 20, 21, and 22, 1954.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons. (1888) *President,* Herbert E. Schmitz, Chicago. *Secretary,* Frank R. Lock, Bowman Gray School of Medicine, Winston-Salem, N. C. Annual meeting, Sept. 9, 10, and 11, 1954.

Central Association of Obstetricians and Gynecologists. (1929) *President,* William O. Johnson. *Secretary,* Harold L. Gainey, 116 S. Michigan Ave., Chicago 3, Ill.

South Atlantic Association of Obstetricians and Gynecologists. (1938) *President,* H. Hudnall Ware, Richmond, Va. *Secretary,* John C. Burwell, Jr., 416 Jefferson Bldg., Greensboro, N. C. Next meeting, Hollywood Beach Hotel, Hollywood Beach, Fla., Jan. 14, 15, and 16, 1954.

A. M. A. Section on Obstetrics and Gynecology. *Chairman,* Bernard J. Hanley, Los Angeles, Calif. *Secretary,* D. Frank Kaltreider, University Hospital, Baltimore, Md. Next meeting, San Francisco, Calif., June 21-25, 1954.

Society of Obstetricians and Gynaecologists of Canada. (1944) *President,* W. G. Cosbie, Toronto, Ont. *Secretary,* Robert B. Meiklejohn, Suite 334, Toronto Western Hospital, Toronto. Next meeting, Harrison Hot Springs, B. C., June 11-13, 1954.

Akron Obstetrical and Gynecological Society. (1946) *President,* Harold Klingler. *Secretary,* Charles V. Bowen, Jr., 925 Second National Bldg., Akron 8. Meetings, third Friday of month, October, January, April, and July.

Alabama Association of Obstetricians and Gynecologists. (1940) *President,* J. C. Hope, Jr. *Secretary,* O. M. Otts, Jr., 1701 Springhill Ave., Mobile. Meetings, November and April.

Alameda County Gynecological Society. (1951) *President,* George C. Calvin. *Secretary,* Victor E. Koerper, 431 30th St., Oakland, Calif. Meetings, fourth Wednesday of each month, except July, August, and December.

Arkansas Obstetrical and Gynecological Society. (1953) *President,* Eugene T. Ellison, Texarkana. *Secretary,* Robert W. Ross, 908 Donaghey Bldg., Little Rock. Meetings, spring and fall.

Birmingham Obstetrical and Gynecological Society. (1949) *President,* S. Buford Word. *Secretary,* Josiah C. Carmichael, 1117 S. 22nd St., Birmingham. Meetings, quarterly.

Boston, Obstetrical Society of. (1861) *President,* Benjamin Tenney, Jr. *Secretary,* A. Gordon Gauld, 1180 Beacon St., Brookline 46, Mass. Meetings, third Tuesday in September, October, November, January, February, and March, Harvard Club, Boston. Tri-city meeting, third Tuesday of April.

Bronx Gynecological and Obstetrical Society. (1924) *President,* Mark Daniel. *Secretary,* Alex Charlton, 1749 Grand Concourse, New York 53, N. Y. Meetings, fourth Monday, October, November, January, February, March, and April.

Brooklyn Gynecological Society. (1890) *President,* J. Edward Hall. *Secretary,* Leslie H. Tisdall, 615 Third St., Brooklyn 15. Meetings, third Wednesday, October, November, January, February, March, April, and May.

Buffalo Obstetrical and Gynecological Society. (1946) *President,* Harry LaForge. *Secretary,* Louis A. Trippe, 511 Lafayette Ave., Buffalo. Meetings, first Tuesday, October through May.

Central New York Association of Gynecologists and Obstetricians. (1938) *President,* Merton Hatch. *Secretary,* Vincent J. Hemmer, Syracuse Medical Arts Bldg., Syracuse. Meetings, second Tuesday, January, March, May, September, and November.

Chicago Gynecological Society. (1878) *President,* Henry Buxbaum. *Secretary,* Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3. Meetings, third Friday, October through June, Hotel Knickerbocker.

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*Changes, omissions, and corrections should be sent to the publisher, The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo. The number after the Society's name is the year of founding. For further information, address the respective secretaries.

Cincinnati Obstetrical Society. (1876) *President,* Richard D. Bryant. *Secretary,* Robert R. Pierce, 116 William Howard Taft Rd., Cincinnati 19. Meetings, third Thursday, September through May.

Cleveland Society of Obstetrics and Gynecology. (1947) *President,* G. Keith Folger. *Secretary,* Eduard Eichner, 10465 Carnegie Ave., Cleveland 6. Meetings, fourth Monday, September, November, January, March, and May.

Columbus Obstetric-Gynecologic Society. (1944) *President,* Robert Daly. *Secretary,* Leonard B. Greentree, 350 E. Broad St., Columbus 15. Meetings, last Wednesday of month, September through May.

Dallas-Fort Worth Obstetrical and Gynecological Society. (1948) *President,* Oren Prejean. *Secretary,* D. G. Harrel, 220 W. Oakenwald, Dallas. Meetings, spring and fall.

Dayton Obstetrical and Gynecological Society. (1937) *President,* E. W. Smith. *Secretary,* M. V. Lingle, 1040 Fidelity Bldg., Dayton 2, Ohio. Meetings, third Wednesday, September through May.

Denver Gynecological and Obstetrical Society. (1942) *President,* Harold J. von Detten. *Secretary,* Raymond Chatfield, 1809 E. 18th Ave., Denver 6, Colo. Meetings, first Monday of every month, unless otherwise notified.

El Paso County Obstetrical and Gynecological Society. (1948) *President,* Erich Spier. *Secretary,* Alvin L. Perry, 209 Medical Arts Bldg., El Paso, Texas. Meetings, first Thursday of each month.

Florida Obstetric and Gynecologic Society. (1948) *President,* Ferdinand Richards. *Secretary,* J. C. Taylor, 1022 Park St., Jacksonville. Meetings, December and April.

Georgia State Obstetrical and Gynecological Society. (1951) *President,* Hugh Bickerstaff, Columbus. *Secretary,* Eugene L. Griffin, Atlanta. Meetings semiannually.

Harris, John Warton, Obstetrical Society. (1953) *President,* Madeline J. Thornton. *Secretary,* Alice D. Watts, 324 E. Wisconsin Ave., Milwaukee 2, Wis.

Honolulu Obstetrical and Gynecological Society. (1947) *President,* Satoru Nishijima. *Secretary,* James T. S. Wong, 1415 Kalakaua Ave. Meetings, third Monday of each month at the Mabel Smyth Memorial Bldg.

Houston Obstetrical and Gynecological Society. (1939) *President,* T. R. Hannon. *Secretary,* Murphy D. Stevenson, 807 Hermann Professional Bldg., Houston. Meetings, first Tuesday each month, October through June.

Indianapolis Obstetrical and Gynecological Society. (1947) *President,* Foster Hudson. *Secretary,* Paul F. Muller, 3311 N. Meridian St., Indianapolis. Meetings, first Wednesday in February, April, and October.

Interurban Obstetrical and Gynecological Society. (1949) *President,* H. Dover, Ottawa, Ont. *Secretary,* E. R. Duggan, 16 N. Goodman St., Rochester 7, N. Y. Meeting, Oct. 2, 1954, Ottawa.

Iowa Obstetric and Gynecologic Society. *President,* J. D. Lutton, Sioux City. *Secretary,* William C. Keettel, State University of Iowa Hospitals, Iowa City. Meetings, April 27 and 28, 1954, Des Moines, and October, Iowa City.

Kansas City Gynecological Society. (1922) *President,* H. M. Floersch. *Secretary,* James E. Keeler, 4301 Main St., Kansas City, Mo. Meetings, last Thursday, September, November, January, and March, and first Thursday in May.

Kentucky Obstetrical and Gynecological Society. (1947) *President,* Leon Higdon, Paducah. *Secretary,* George McClure, Danville. Annual Meeting, Frankfort, April 1 and 2, 1954.

Los Angeles Obstetrical and Gynecological Society. (1914) *President,* Stirling Pillsbury. *Secretary,* Samuel M. Martins, 825 S. Alvarado, Los Angeles 57. Meetings, second Tuesday, September, November, January, March, and May.

Louisville Obstetrical and Gynecological Society. *President,* Glenn W. Bryant. *Secretary,* J. O. H. Simrall, 1720 Heyburn Bldg., Louisville. Dinner meetings, fourth Monday, September, October, November, January, February, March, April, and May.

Madison Obstetrical and Gynecological Society. (1950) *President* and *Secretary,* Lee B. Stevenson, 16 S. Henry St., Madison 3, Wis. Meetings, first Tuesday each month except July, August, and September.

Maryland, Obstetrical and Gynecological Society of. (1929) *President,* John Whitridge. *Secretary,* W. Drummond Eaton, 11 E. Chase St., Baltimore 2. Meetings, second Thursday, October, December, February, and April.

Memphis Obstetrical and Gynecological Society. (1950) *President,* Cecil Warde. *Secretary,* William F. Mackey, 1374 Madison Ave., Memphis. Meetings, October, November, January, March, and May.

Miami Obstetrical and Gynecological Society. (1946) *President,* George A. Mitchell. *Secretary,* Henry Caffee, Douglas Entrance Apt., Coral Gables. Meetings, second Thursday, January, March, May, and November.

Michigan Society of Obstetricians and Gynecologists. (1924) *President,* R. L. Haas. *Secretary,* C. Paul Hodgkinson, 2799 W. Grand Blvd., Detroit 2. Meetings, first Tuesday, October, November, December, February, March, April, and May.

Minnesota Obstetrical and Gynecological Society. *President,* Arthur B. Hunt. *Secretary,* Rodney F. Sturley, 350 Saint Peter St., St. Paul. Meetings, spring and fall.

Mississippi Obstetrical and Gynecological Society. (1947) *President,* William B. Wiener, Jackson. *Secretary,* J. A. K. Birchett, Jr., The Street Clinic, Vicksburg. Meetings May and October.

Mobile Obstetrical and Gynecological Society. (1949) *President,* H. B. Dowling. *Secretary,* J. R. Mighell, 1302 Goverment St., Mobile. Meetings, second Thursday, January, April, July, and October.

Montana Obstetrical and Gynecological Society. (1946) *President,* S. N. Preston, Missoula. *Secretary,* Leonard G. Brewer, 212 N. Higgins Ave., Missoula.

Nassau Obstetrical Society. (1944) *President,* Arthur F. Wright. *Secretary,* David E. Warden, 22 Oakwood Road, Huntington, N. Y. Meetings, second Monday, October, December, February, and April.

New England Obstetrical and Gynecological Society. (1929) *President,* Joel M. Melick, Worcester, Mass. *Secretary,* Carmi R. Alden, 270 Commonwealth Ave., Boston 16, Mass.

New Haven Obstetrical and Gynecological Society. (1946) *President,* Orvan W. Hess. *Secretary,* Edward B. O'Connell, 1427 Chapel St., New Haven, Conn. Meetings, third Tuesday, September, November, January, March, and May.

New Jersey Obstetrical and Gynecological Society. (1947) *President,* Albert B. Davis. *Secretary,* Felix H. Vann, 242 Engle St., Englewood. Meetings, October and April.

New Mexico Obstetrical and Gynecological Society. (1947) *President,* Randolph V. Seligman. *Secretary,* Charles H. Rundles, Medical Arts Square, Albuquerque. Meetings, last Thursday of each month.

New Orleans Obstetrical and Gynecological Society. (1924) *President,* E. W. Nelson. *Secretary,* Abe Mickal, 1413 Richards Bldg., New Orleans 12. Meetings, monthly, September through May.

New York Obstetrical Society. (1863) *President,* Ralph L. Barrett. *Secretary,* Henry S. Acken, Jr., 34 Prospect Park West, Brooklyn 15. Meetings, second Tuesday from October through May.

North Carolina Obstetrical and Gynecological Society. (1932) *President,* Richard L. Pearse, Durham. *Secretary,* Adam Thorp, Rocky Mount. Meeting last weekend in April, 1954.

North Dakota Society of Obstetrics and Gynecology. (1938) *President,* Frank DeCesare. *Secretary,* John Gillam, Box 1388, Fargo. Meetings, spring and fall.

Northeastern New York Obstetrical and Gynecological Society. (1935) *President,* William B. Van Auken. *Secretary,* Rudolph F. Amyot, 28 First St., Troy, N. Y. Meetings, third Thursday of January, May, and October.

Oklahoma City Obstetrical and Gynecological Society. (1940) *President,* Thomas C. Points. *Secretary,* W. K. Hartford, 1111 N. Lee St., Oklahoma City 3. Meetings, second Wednesday, October, December, February, and April.

Omaha Obstetrical and Gynecological Society. (1947) *President,* John J. Freymann. *Secretary,* W. Riley Kovar, 1120 Medical Arts Bldg., Omaha 2. Meetings, third Wednesday, January, March, May, September, and November.

Oregon Society of Obstetricians and Gynecologists. *President,* George Lage. *Secretary,* J. Oppie McCall, Jr., 812 S. W. Washington, Portland 5. Meetings, third Friday, October through May, except December.

Pacific Coast Obstetrical and Gynecological Society. (1931) *President,* Emil J. Krahulik. *Secretary,* Donald G. Tollefson, 511 S. Bonnie Brae St., Los Angeles 57. Meeting, Oct. 27-30, 1954.

Pacific Northwest Obstetrical and Gynecological Association. (1947) *President,* William M. Wilson, Portland, Ore. *Secretary,* Earl L. Hall, 410 Central Ave., Great Falls, Mont. Meeting, second week of June, 1954, Portland, Ore.

Philadelphia, Obstetrical Society of. (1868) *President,* Benjamin Leff. *Secretary,* Paul O. Klingensmith, 133 S. 36th St., Philadelphia 4. Meetings, first Thursday, October through May.

Pittsburgh Obstetrical and Gynecological Society. (1934) *President,* David Katz. *Secretary,* William E. Gibson, 1010 Center St., Pittsburgh 21. Meetings, first Monday, October through May, except January.

Portland Society of Obstetricians and Gynecologists. *President,* Jack W. Dowsett. *Secretary,* George H. Lage, 453 Medical Arts Bldg., 1020 S. W. Taylor St., Portland 5, Oregon. Meetings, fourth Wednesday, September through June.

Queens Gynecological Society. (1948) *President,* William Filler. *Secretary,* George Schaefer, 98-11 Queens Blvd., Forest Hills, N. Y. Meetings, second Wednesday, October, December, February, April, and June.

Rochester Obstetrical and Gynecological Society. (1939) *President,* Louis Iuppa. *Secretary,* Fred Fumia, 39 N. Goodman St., Rochester, N. Y. Meetings, September, December, March, and June.

St. Louis Gynecological Society. (1924) *President,* Leo Hartnett. *Secretary,* W. H. Vogt, Jr., 508 N. Grand Blvd., St. Louis 3. Meetings, second Thursday, October, December, February, and April.

San Antonio Obstetrical and Gynecological Society. *President,* G. G. Passmore. *Secretary,* Frank M. Posey, Jr., 640 Moore Bldg. Meetings, first Monday of the month.

San Diego Gynecological Society. (1937) *President,* Ralph L. Hoffman. *Secretary,* George H. Derieux, 233 A St., San Diego, Calif. Meetings, second Monday of each month.

San Francisco Gynecological Society. (1929) *President,* Donald W. de Carle. *Secretary,* Edmund F. Anderson, 2445 Ocean Ave., San Francisco 27, Calif. Meetings, second Friday, October through May.

Seattle Gynecological Society. (1941) *President,* Robert H. Stewart. *Secretary,* Charles S. Fine, 340 Stimson Bldg., Seattle 1, Wash. Meetings, third Wednesday of each month, September through June except February and December.

South Carolina Obstetrical and Gynecological Society. (1946) *President,* Arthur L. Rivers, Charleston. *Secretary,* Lawrence L. Hester, Jr., 16 Lucas St., Charleston. Meetings, spring and fall.

Southwest Obstetrical and Gynecological Society. (1951) *President,* William Buster McGee. *Secretary,* Jesse A. Rust, Jr., 3115 University Ave., San Diego 4, Calif. Annual fall meeting, October or November.

Texas Association of Obstetricians and Gynecologists. (1930) *President,* D. D. Wall, San Angelo. *Secretary,* Carey Hiett, 815 Fifth Ave., Ft. Worth. Meeting, Waco, Texas, February 19 and 20, 1954.

Utah Obstetrical and Gynecological Society. (1948) *President,* M. S. Sanders. *Secretary,* Von G. Holbrook, 508 East South Temple, Salt Lake City 2. Meetings, to be announced.

Virginia Obstetrical and Gynecological Society. (1936) *President,* Chester L. Riley. *Secretary,* Chester D. Bradley, 2914 West Ave., Newport News. Meetings, April and October.

Washington Gynecological Society. (1933) *President,* Samuel Dodek. *Secretary,* J. B. Sheffery, 1801 K St., N. W., Washington, D. C. Meetings, Jan. 20, March 27, and May 5, 1954.

Washington State Obstetrical Association. (1936) *President,* Philip Kyle, Tacoma. *Secretary,* Robert Campbell, Stimson Bldg., Seattle 1. Meetings, April and October.

Wisconsin Society of Obstetrics and Gynecology. (1940) *President,* George H. Stevens. *Secretary,* Dean D. Willson, 92 East Division St., Fond du Lac. Meetings, May and October.